MEDICAL PROCEEDINGS

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Pfizer

INTERNATIONAL

medical news bulletin

Current Developments in the Fields of Antibiotics, Hormones, Nutrition and Clinical Medicine

Prepared for Physicians by the Medical Department of Pfizer International, Inc., 25 Broad Street, New York 4, N.Y., U.S.A.

Vol. 111, No. 9, 1956

ANTIBIOTIC NEWS AND NOTES

TERRAMYCIN-SF®* EFFECTS "REMARKABLY RAPID" RESPONSE IN RESPIRATORY INFECTIONS - Forty-three of 45 patients with various infections (chiefly of the respiratory tract) showed "excellent" results and 2 "improved rapidly" after treatment with 1 Gm. Terramycin a day together with stress vitamins. In 35 of the 45 patients, temperature returned to normal within 24 hours. Daskal[1] feels that the patients treated in this series, compared to other similar cases treated with an antibiotic alone, not only responded "more rapidly" but had a "much shorter convalescent period. . . ." The medication was also even "better tolerated" than is usual. "Further, the common companions of an infectious febrile illness, such as lassitude, irritability, anorexia, fatigability, and weakness, either did not occur at all or were of minimal and inconsequential severity." Because of the established experimental and clinical evidence that stress vitamins are of vital importance in reparative and recuperative efforts in patients subjected to serious surgical, traumatic, or infectious diseases, Daskal believes that the antibiotic-vitamin combination "represents a most valuable addition to the physician's armamentarium."

THERAPY OF URINARY INFECTIONS - In 71 patients with urinary tract infections caused by 98 different organisms, tetracycline** was "most effective" against the pyogenic group. Marks and colleagues[2] found it also "effective" in the majority of infections due to B. coli and the coliform group of organisms, and they observed a "high correlation" between in vitro sensitivity studies and therapeutic response.

Reporting on present therapy of recalcitrant urinary tract infections, another investigator, Lich,[3] recommends that antibiotic therapy should be started only after sensitivity studies dictate the drug of choice. "There is nothing to be gained by instituting immediate therapy when the situation has been of long standing."

PROPHYLACTIC TERRAMYCIN®† OPHTHALMIC SOLOUTION IS "SAFE" AND "MORE DESIRABLE" than silver nitrate for ophthalmia neonatorum, states Chapman.[4] A series of 2000 births was divided into 2 groups of 1000 babies, each receiving two drops of either solution into each eye within the first 48 hours after birth. Results showed that the large number of chemical reactions attributed to the silver solution can be

*Brand of oxytetracycline with vitamins
**Available from Pfizer as Tetracyn®
†Brand of oxytetracycline

decreased by the use of an ophthalmic Terramycin solution. The antibiotic protects the eyes from pathogens as well as or better than the silver nitrate solution. Chapman, therefore, feels that Terramycin "would not only be a safe but a more desirable replacement therapy" in the routine treatment of eyes in newborn babies.

DIHYDROSTREPTOMYCIN. "THERAPEUTIC TRIUMPH" IN STAPHYLOCOCCAL SEPTICEMIA - A patient with Staphylococcus aureus septicemia developing after dental surgery, showed "rather dramatic improvement" when dihydrostreptomycin was started after other antibiotics had failed. The complicating meningitis, endocarditis, and septic embolism were cured by the treatment, a "therapeutic triumph" against an organism heretofore considered lethal in the majority of cases. Whole blood transfusions were given as a supportive measure. "It is ironic," says Di Fiore,[5] "that our in vitro sensitivity tests performed on the first and only positive blood culture revealed inhibition of growth only in the presence of streptomycin. Because these tests were so atypical and confusing and because of the usual failure of streptomycin to influence staphylococcal infections, streptomycin therapy was left as a last resort." The author recommends aggressive and intensive treatment against this virulent organism.

REPORT FROM ARGENTINA: TERRAMYCIN INJECTIONS "SPECTACULAR" IN PROSTATITIS - Terramycin in distilled water injected into the prostate produced "excellent or good" results in 93 of 100 patients with prostatitis which had not responded to other forms of treatment. Mosqueira[6] describes a "simple and safe procedure" for injection: 500 mg. Terramycin in 100 cc. distilled water is applied, under anesthesia (thiopental sodium), locally once a week by injection through the rectum into the prostate. "Spectacular" results were achieved after an average of 4 treatments. Author attributes the mechanism of recovery not only to the antimicrobial action of the antibiotics, but also to its "irritant action which partially scleroses the gland and, thus, reduces its inflammatory state and volume." No complications were encountered in this series.

ANTIBIOTIC PROPHYLAXIS IN TRAUMA - "In the event of an atomic disaster or a situation in which there would be a great delay in initial debridement of wounds, antibiotic prophylaxis would be of cardinal importance." Therefore, Strawitz and colleagues[7] studied the plasma levels of 65 severely injured Korean battle casualties after intramuscular injection of aqueous procaine penicillin. They found most concentrations to be "well above the recommended minimal therapeutic level for most penicillin-sensitive infections," yet below those of control subjects. The levels ranged up to 1.8 U./ml. in 39 patients (21 hypotensives) receiving 300,000 U. and up to 2.2 U./ml. in 26 patients (8 hypotensives) receiving 600,000 U. "The levels obtained in hypotensive patients did not differ significantly from the levels in the normotensive group."

ANTIBIOTICS AROUND THE WORLD

AUSTRIA: BRONCHOSCOPIC TERRAMYCIN INSTILLATIONS "OPTIMAL" IN BRONCHIECTASIS - "Successful" results were obtained in the majority of 100 patients (53 preoperative) with bronchiectasis after Terramycin instillations, supplemented by intravenous admininstration and aerosol inhalations of the antibiotic. Stolzer (Univ. Graz)[8] asserts that the instillation results in an "optimal and direct effect of Terramycin . . . on the site of the disease." The treatment prevented appearance of complications, decreased cough and sputum, improved general conditions and restored working ability in many instances. "...with Terramycin irrigation of the bronchial tree, marked improvement or surgical fitness was obtained in every stage and without regard to the extent of the disease."

AUSTRALIA: TERRAMYCIN OINTMENT PREVENTS NEONATAL STAPHYLOCOCCAL INFECTION - Clarke and colleagues[9] report a 21.5% incidence of neonatal infections of the skin caused by Staphylococcus pyogenes among 200 babies born from September 5 to December 11, 1954, at the Maitland Hospital, New South Wales. In order to prevent this occur-

rence, authors started using 1% Terramycin inserted t.i.d. into the anterior nares to treat the nasal carrier state of the hospital staff. "Very considerable improvement" followed this simple procedure, and "pronounced and lasting reduction" of the disease was noted.

AUSTRIA: TERRAMYCIN ABSORPTION HELPED BY TRYPSIN IN AEROSOL THERAPY - Hammerl and Huber[10] observe that the effect of Terramycin aerosol therapy was "predominantly" a local one, when the medication was given to 210 patients (normal controls as well as patients with bronchitis). To determine what would most aid absorption of the antibiotic, they tested various pharmaceuticals, and found that trypsin inhalations before aerosol treatment provided "the most favorable combination...."

IRAQ: DIHYDROSTREPTOMYCIN "SPECIFICALLY EFFECTIVE" AGAINST LEISHMANIASIS - In treating 800 patients with dihydrostreptomycin, Kochs[11] finds it a means of "such excellent antibiotic activity against Leishmania tropica that it can at present be considered the drug of choice in cutaneous leishmaniasis." Within a few days of intramuscular or intrafocal treatment, the leishmania usually disappeared and almost all patients were cured.

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HORMONES

MOST EFFECTIVE DOSAGES OF PREDNISOLONE* and prednisone in four major allergic syndromes were discussed by Brown and Seideman at the 105th Annual Meeting of the American Medical Association in Chicago.[1] After studying a large series of patients, the authors feel that the following dosage schedules are most effective: in hay fever 15 to 20 mg. a day for 2 to 3 weeks after the onset of moderately severe symptoms; in perennial allergic rhinitis, which had not responded to any other means of therapy, initial dosage of 10 mg. q.i.d., tapered off gradually to a maintenance dose of 5 mg. b.i.d. In bronchial asthma, 40 mg. a day for the first 48 hours and then decreased gradually by 2½ mg. a day to a maintenance dose of 10 to 15 mg. daily. In allergic dermatoses, initial dosage of 30 to 40 mg. a day for 3 or 4 days depending upon the severity of symptoms and gradually reduced to a maintenance dose of 2½ mg. a day to as little as 5 mg. twice a week. The two steroids are most effective in self-limiting syndromes such as ragweed pollinosis, acute contact dermatitis, and acute urticaria, which are conditions requiring brief treatment and a minimum of supervision.

PREDNISOLONE, PREDNISONE EFFICACIOUS IN LUPUS ERYTHEMATOSUS - Treatment with prednisolone or prednisone effected abatement of fever within 24 to 48 hours in all of 31 patients with active systemic lupus erythematosus. Joint pains disappeared within several days, and pleural effusions, as well as cutaneous lesions, subsided within one to two weeks. Dubois[2] recommends an ulcer regimen when the patients are receiving over 10 mg. a day of either steroid and a low sodium diet when

*Prednisolone supplied by Pfizer as Deltacortril.® 5 mg. tablets, white, scored, in bottles of 10, 20 and 100.

they are taking over 50 mg. a day for a long period of time. The average maintenance dose in this series was 22 mg. a day of either steroid.

PREDNISOLONE SUCCESSFUL IN BRONCHIAL ASTHMA - Complete success was obtained with prednisolone in 9 of 10 patients with bronchial asthma. Martini and colleagues[3] used an initial dose of 44.5 mg., and an average maintenance dose of 8 mg. a day. Therapy generally stopped after about 7 days of maintenance dose.

GERMANY: DELTACORTRIL® "EFFECTIVE" IN RHEUMATOID ARTHRITIS - Nine of 10 patients with primary or secondary rheumatoid arthritis showed "objective and subjective improvement" 24 hours after Deltacortril treatment. "Clinically, satisfactory effect on joint mobility was seen in all cases. The patients reported marked decrease of pain.... Acute or subacute inflammatory irritative conditions of joints disappeared mainly within 36 hours...." Golz[4] considers the steroid an "effective drug, relatively simple to use."

GREAT BRITAIN: DELTACORTRIL "ENCOURAGING" IN NEPHROSIS - The immediate results of Deltacortril treatment in nephrosis are "encouraging and significantly superior" to those obtained with either corticotropin or cortisone. Within 6 days, the steroid effected diuresis and a striking decrease of albuminuria in 4 children with nephrosis. Arneil[5] considers it likely that "little progress would be made in treating nephrosis until some method of diminishing albuminuria could be found." Since Deltacortril seems to have this property, he recommends high initial dosage to eliminate albuminuria, followed by such dosage as keeps the urine clear thereafter. Since albuminuria is a sign of grave prognostic significance, immediate treatment with Deltacortril is urged.

GREAT BRITAIN: HYDROCORTISONE PREVENTS THROMBOPHLEBITIS IN PROTRACTED INFUSIONS - In a preliminary communication, Polak[6] observes that patients receiving systemically large doses of hydrocortisone seem less liable than others to develop phlebitis after protracted infusions - an effect which was attributed to the ability of this hormone to suppress inflammation. "Therefore, when hydrocortisone alcohol became available, it was decided to test the power of this steroid, added to an intravenous infusion, to prevent or to suppress phlebitis, advantage being taken of the fact that a very high local concentration of hydrocortisone could be produced in the vein receiving the infusion by a dose which would be without systemic effect." Three patients were selected in whom there was an indication for the intravenous administration of hypertonic dextrose, and they were given 20% dextrose solution containing 0.001% (10 mg./litre) of hydrocortisone. No clinical evidence of thrombophlebitis developed in any of these patients during or after the 20% dextrose hydrocortisone infusions.

FRANCE: PREDNISONE POINTS TO "NEW THERAPEUTIC ORIENTATION" IN MULTIPLE SCLEROSIS, say Claisse and colleagues.[7] The steroid effected "varying degrees of improvement" in 23 of 56 patients, mainly with advanced multiple sclerosis. Prednisone "seems to bring therapeutic progress," and "appreciable" improvement in the general condition as well as in neurologic disturbances of the disease.

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Address for Medical Enquiries:
PFIZER LABORATORIES SOUTH AFRICA (PTY.) LTD.
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REDAKSIONEEL · EDITORIAL

BLUT-POLITIK

Die besluit van die Geneeskundige Raad (ná 'n debat agter geslote deure op sy Septembervergadering) om die afkondiging aan te beveel van regulasies wat aandring op die rasse-identifikasie van menslike bloed wat vir oortappingsdoeleindes bedoel is, sal mediese wetenskaplikes nie alleen in Suid-Afrika nie maar ook in die res van die wêreld onthuts.

In alle billikheid teenoor die Geneeskundige Raad moet daar erken word dat hierdie laakbare ekskursie in die moderne politieke sfeer nie van stapel gestuur is binne die Raad self nie. Die ontwerpregulasies is na die Raad verwys as deel van die prosedure in gevolge waarvan die Minister van Gesondheid die Geneeskundige Raad raadpleeg (soos vereis deur die Wet op Geneeshere, Tandartse en Aptekers) oor sake rakende die doeltreffendheid van die regulasies wat betrekking op bloedskenkerdienste het.

Dit is verstaanbaar dat lede van die Geneeskundige Raad, manne met 'n morele en wetenskaplike gewete, erg in die verleentheid gebring is deur die oorspronklike ontwerpregulasies wat blykbaar deur amptenare van die Unie-gesondheidsdepartement opgestel is, en hierdie regulasies so stuitend gevind het dat hulle begin soek het na 'n kompromis in gevolge waarvan die ontwerpregulasies gewysig en in hul mins aanstootlike vorm deur die Raad voorgelê kon word. Maar hierdie aanval op die wetenskap kan nie gekondoneer word deur 'n kleinere intellektuele belediging nie.

Tot op hede was die enigste gegewens wat vereis is vir die identifikasie van bloed wat vir oortappingsdoeleindes gebruik word die wetenskaplike inligting wat nodig is om die toediening van daardie bloed so veilig as moontlik te maak. Al doen ons ons verbeelding ook hoeveel geweld aan kan ons nie sê dat die rasse-identifikasie van 'n bottel bloed die bloedoortappingsproses enigsins

The decision of the Medical Council (after a secret debate at its September meeting) to recommend the promulgation of regulations requiring the racial identification of human blood intended for transfusion, will distress medical scientists not only in South Africa but also in the rest of the world.

In fairness to the Medical Council, it should be recognized that this lamentable excursion into the politics of the day was not initiated by a primary act within the Council itself. The draft regulations were referred to the Council as part of the procedure whereby the Minister of Health consults the Medical Council (as required by the Medical, Dental and Pharmacy Act) in matters touching regulations affecting blood donor services.

It is understandable that members of the Medical Council, men of moral and scientific conscience, found themselves in a dilemma when faced with the original draft regulations apparently prepared by officers of the Union Health Department, and regarded them as so repugnant that they sought a compromise whereby the draft regulations would be modified and submitted by the Council in their least offensive form. But this assault upon science cannot be condoned by lesser degrees of intellectual insult.

Until now, the only data required to identify blood for human transfusion was scientific information intended to ensure the greatest safety in the administration of that blood. By no conceivable stretch of the imagination can the racial identification of a bottle of blood help to make blood transfusion

veiliger maak nie. (Ons moet gedagtig bly aan die feit dat die onlangse aandrang op die hersiening van die regulasies betreffende die oortapping van bloed en bloedprodukte voortgespruit het uit 5 tragiese sterfgevalle volgende op die toediening van besmette bloed aan pasiënte in Kaapstad.)

Weens die titel en die statutêre status van die Geneeskundige Raad kan die publiek sy optrede rederlikerwys vertolk as 'n aanduiding dat daar die een of ander wetenskaplike grond vir die rasse-etikettering van menslike bloed is. Dis egter 'n bekende feit dat daar geen die geringste bewys is ter ondersteuning van die standpunt dat daar enige denkbare gevaar bestaan (mits die bloed verenigbaar en onbesmet is) as bloed van die een lid van die menslike ras in 'n ander lid van daardie ras oorgetap word nie, en dit is betreurenswaardig dat die Raad se optrede miskien tot gevolg sal hê dat so 'n mening posvat onder onkundiges en bevooroordeeldes.

Ons is die mening toegedaan dat die Raad homself mislei en tot buite die grense van sy tegniese en deskundige sfeer gegaan het toe hy ingewillig het om oorweging aan hierdie regulasies te verleen. In 'n sekere sin is die regulasies op die Raad afgedwing, maar ons meen dat hierdie verhewe liggaam hulle moes beskou het (in die vorm waarin hulle voorgelê is) as iets wat buite die bestek van die Geneeskundige Raad se behoorlike funksies val. In die omstandighede sou die Raad verstandig gehandel het as hy geweier het om hom in te meng met die anti-wetenskaplike gedeeltes van die regulasies, want die Raad se goedkeuring van hierdie gedeeltes kan alleen aanleiding gee tot verontrusting en verleentheid onder almal wat waarde heg aan die beginsels van die wetenskaplike metodes wat die hoeksteen van die mediese praktyk vorm.

Maar die aanbeveling dat hierdie regulasies afgekondig moet word, bring ook 'n verdere tragedie mee—die feit, naamlik, dat hulle heeltemal onnodig is. Soos daar tydens 'n openbare bespreking van hierdie ontwerpregulasies vroeër in die jaar in Durban verklaar is, sorg die Bloedoortappingsdienste in hierdie land dat geen bloed van nie-blanke skenkers in blanke ontvangers oorgetap word nie uit agting vir die bekende vooroordeel van die meeste blanke Suid-Afrikaners wat hierdie besondere aangeleentheid betref. Hoe dit ook al sy, dit is een ding as die skenkerdienste so 'n maatskaplike konvensie in ag neem (mits diegene wat bloed dringend nodig het nie daardeur geprejudiseer word nie), maar dit is heeltemal 'n ander ding as die Mediese Raad aanbeveel dat die rasse-identiteit van die bloed kragtens wet op die houer aangedui moet word.

Die *reductio ad absurdum* van hierdie beginsel moet dan ook die rasse-identifikasie van bloedderivate vereis, bv. plasma, serum, fibrinogeen, albumien, die globuliene, ens. Trouens, die ontwerpregulasies soos voorgelê deur die Unie-gesondheidsdepartement maak voorsiening vir die onderskeidende etikettering van hierdie produkte op 'n rasse-grondslag. Tot dusver is die merendeel van hierdie stowwe uit die buiteland ingevoer waar daar geen rasse-diskriminasie is by die keuse van bloed vir hierdie vervaardigingsdoeleindes nie. Gaan ons nou die invoer van hierdie produkte verbied tensy bewys gelewer kan word dat hulle geëtiketteer is ooreenkomstig ons vereistes?

Bloed is bloot een van ons mees elegante en fisiologiese inplantingsweefsels. Gaan dit nou die lot wees van alle ander inplantings wat in die

safer. (It should be recalled that the recent impetus to revise regulations governing the transfusion of blood and blood products was provided by 5 tragic deaths following the administration of contaminated blood to patients in Cape Town.)

The action of the Medical Council, because of its title and statutory status, can quite reasonably be interpreted by the public to mean that there is some kind of scientific basis for the racial labelling of human blood. There is, as is well known, not a tittle of evidence to support the view that there can be any conceivable danger (provided the blood is compatible and not diseased) in giving blood from one member of the human species to another member of that species, and it is regrettable that the Council's action may provide an opportunity for such a view to gain a footing amongst the ignorant and the prejudiced.

It is our submission that the Council misdirected itself and travelled outside its technical and expert sphere in agreeing to receive these regulations for consideration. In a sense, the regulations were foisted on the Council, but we feel that this august body should have regarded them, in the form in which they were submitted, as outside the ambit of the Medical Council's proper functions. In these circumstances, the Council would have been wiser to decline to handle the anti-scientific portions of the regulations, as their action in endorsing them could only lead to alarm and distress amongst all who set store by the principles of the scientific method which forms the very basis of the practice of medicine.

The further tragedy involved in the recommendation that these regulations be promulgated lies in the fact that they are totally unnecessary. As was stated at the public discussion of these draft regulations in Durban earlier this year, the Transfusion Services in this country do not transfuse blood from non-White donors to White recipients, in deference to the known prejudices of most White South Africans in this matter. However, it is one thing for the donor services to observe such a social convention (provided those in vital need of blood are not prejudiced thereby) and quite another thing for the Medical Council to recommend that the racial identity of blood be inscribed by law on the container.

The *reductio ad absurdum* of this principle must also require racial identification of blood derivatives, e.g. plasma, serum, fibrinogen, albumin, the globulins, etc. Indeed, the draft regulations presented by the Union Health Department make just such provision for the distinctive labelling of these products on a racial basis. Hitherto, most of these substances have been imported from overseas countries which do not exercise any racial discrimination in the selection of blood for these manufacturing purposes. Is the importation of these products now to be prohibited unless proof can be furnished that they have been labelled in accordance with our requirements?

Blood is merely one of our most elegant and physiological graft tissues. Is it to be the fate of

Suid-Afrikaanse chirurgie gebruik word, om verwyder en afsonderlik gebêre en met 'n rasse-onderskeidingsteken geëtiketteer te word?

Die opstel van sulke regulasies, as hulle dan nodig geag word, behoort die morele en regsverantwoordelikheid van 'n liggaam anders as die Geneeskundige Raad te wees, aangesien die beginsel wat by die saak betrokke is politiek en ideologies is, en nie op die mediese wetenskap berus nie. Met ander woorde, die Raad moes nie toegelaat het dat hy in die politieke strydperk gesleep word nie.

Vir 'n regering is dit moontlik om bloedoortappingsregulasies wat die spot met wetenskaplike beginsels en die morele krag van die Hippokratiese kode dryf, af te kondig en van krag te maak; maar sodanige optrede wat in sy wese suiwer politiek en anti-wetenskaplik is, moet nie 'n professionele liggaam soos die Geneeskundige Raad verstrik nie. Die bepalings is opgestel buite die mure van die Raad en dit is ongelukkig dat hulle ooit binne die mure van die Raad oorweeg is.

Die goeie naam van die Suid-Afrikaanse mediese wetenskap loop ernstige gevaar om 'n dodelike knou op te doen. Die voorgestelde regulasies gaan ongetwyfeld heelwat teenkanting uitlok, heeltemal afgesien van die argumente wat noodwendig uit die beginsels van wetenskaplike denke voortspruit. Ons wil derhalwe by die Minister daarop aandring om twee maal na te dink voordat hy oorgaan tot die afkondiging van hierdie sleg gekonsipieerde en onnodige vereiste wat niks bydra tot bevordering van die saak, die veiligheid of die praktyk van bloedoortapping in die Unie nie, maar inteendeel die mediese professie in hierdie land alleen aan die minagting en hoon van die beskaafde wêreld blootstel.

all other grafts used in South African surgery, that they must also be removed and stored separately and identified with a racially distinctive tag?

The formulation of these regulations, if they are deemed necessary, should be the moral and legal responsibility of a body other than the Medical Council, as the principle involved is a political and ideological one and not one rooted in medical science. The Council should, therefore, not have allowed itself to be dragged into the hurly-burly of political polemics.

A Government may well sponsor and enforce blood transfusion regulations which flout the principles of science and the moral force of the Hippocratic code; but such an action, purely political and anti-scientific in its quality, should not have embroiled a professional body such as the Medical Council. The provisions were conceived outside the walls of the Council and it is most unfortunate that they should ever have been considered within the walls of that Council.

The high reputation of South African medical science is in grave danger of mortal injury. The proposed regulations will undoubtedly provoke considerable opposition, even apart from those arguments that the principles of scientific thinking make imperative. We would therefore urge upon the Minister the need to refrain from proceeding with the promulgation of this ill-conceived and superfluous requirement which does not advance the cause, the safety or the practice of blood transfusion in the Union, and which can only expose the medical profession in this country to the scorn and ridicule of the civilized world.

'N GEVAL MET 'N BYKOMSTIGE DORSALE URETHRA IN DIE MAN

'N BESKRYWING EN BESPREKING

T. MULLER, M.B., CH.B.

Departement van Anatomie, Universiteit van Pretoria, Pretoria

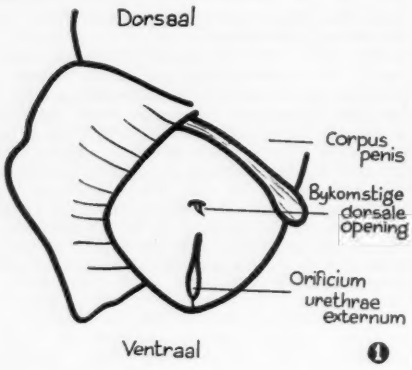
In die ontleedsaal is toevallig 'n paar jaar gelede die aandag gevestig op 'n ekstra buisvormige struktuur in die penis, wat gevind is nadat 'n dwarssnit deur die penis gemaak is. Die blaas en prostaat is versigtig verwyder nadat die penis met die trigonum urogenitale losgesny is langs die rami van die pubis en ischium. Sodoende kon die buisagtige struktuur volledig gevolg word in sy geheel.

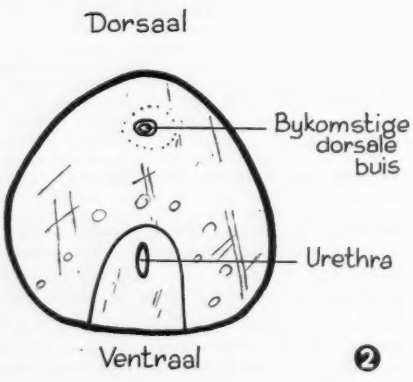
Geskiedenis. Dit was 'n kadawer van 'n ouerige naturel. Die oorsaak van dood was aangegee as tering. Geen vorige geskiedenis kon verkry word wat die urogenitale-stelsel betref nie.

Makroskopiese Bevindinge. Op die glans penis was duidelik sigbaar 'n ekstra opening omtrent 'n kwart duim dorsaal van die orificium urethrae externum. Daar was geen tekens van epispadie nie. (Fig. 1, 1A.) Deur seriële-snitte deur die penis te maak, kan 'n mens die buisvormige struktuur deur die hele lengte van die penis volg. (Fig. 2-6.) Die buisvormige struktuur het sy maksimum grootte bereik omtrent 2 duim agter die punt van die glans, waar dit in die septum penis tussen die 2 corpora cavernosa penis geleë was en hard gevoel het by betasting. Daarna het die buis kleiner geword na agter maar kon gevolg word tot onder die symphysis pubis waar dit digby die vena dorsalis penis (profunda) geleë was. Dit het skynbaar superior ten opsigte van die prostaat verloop en 'n

sagte, dun, buisagtige struktuur kon weer gevolg word oor die anterior gedeelte van die blaas, waar dit doodgeloop het sonder dat enige definitiewe opening of verbinding met die blaas gevind kon word.

Mikroskopiese Bevinding. Histologiese-snitte is gemaak van die penis omtrent 'n halfduim tot 'n duim van mekaar asook van die prostaat en buisagtige struktuur in verhouding tot die anterior gedeelte van die blaas. Vir ongeveer die eerste 3 duim of meer het die buis 'n voering gehad van meerlagige plaveisel-epiteel. Daar was duidelike tekens van chroniese ontsteking. Verder na agter het die buis 'n voering van oorgangs-epiteel





getoon. In die prostaat was geen tekens van 'n ekstra urethra nie. Die buis in verhouding tot die anterior gedeelte van die blaas het oorgangs-epiteel vertoon.

BESPREKING

Hierdie ekstra buisvormige struktuur van die penis het die kenmerke van 'n bykomstige dorsale urethra. 'n Ware dubbele urethra volgens Arnold en Kaylor,[1] is baie seldsaam en is alleen van toepassing op die gevalle waar daar 'n volledige duplikasie van die urethra in een penis is en waar die 2 kanale onafhanklik in die blaas open en parallel verloop sonder

Fig. 1*A.* Die glans penis waarop die orificium urethrae externum ventraal geleë is en die bykomstige opening dorsaal.

enige verbinding met mekaar. Tariff se klassifikasie van bykomstige urethrae word kortliks uiteengesit deur Irwisch en Cook.[2] Die mees algemene tipe van bykomstige urethra open op die dorsum van die penis en nadat dit 'n ent na agter verloop het, eindig dit blind sonder enige verbinding met die urinêre-sisteem. Nové-Josserand[3] verdeel hierdie tipe van bykomstige buis in 4 groepe:

1. Dubbele urethra.
2. Dorsale fistels van die penis.
3. Fistels aan die onderkant van die penis.
4. Blinde fistels van die glans.

Sy eie opinie is, dat 'n dubbele urethra van een penis ook beskou moet word as 'n dorsale fistel van die penis. Die kenmerke van 'n dorsale fistel of bykomstige urethra word as volg gestel:

Hierdie buis open altyd aan die dorsale kant van die penis, partykeer op die glans, maar

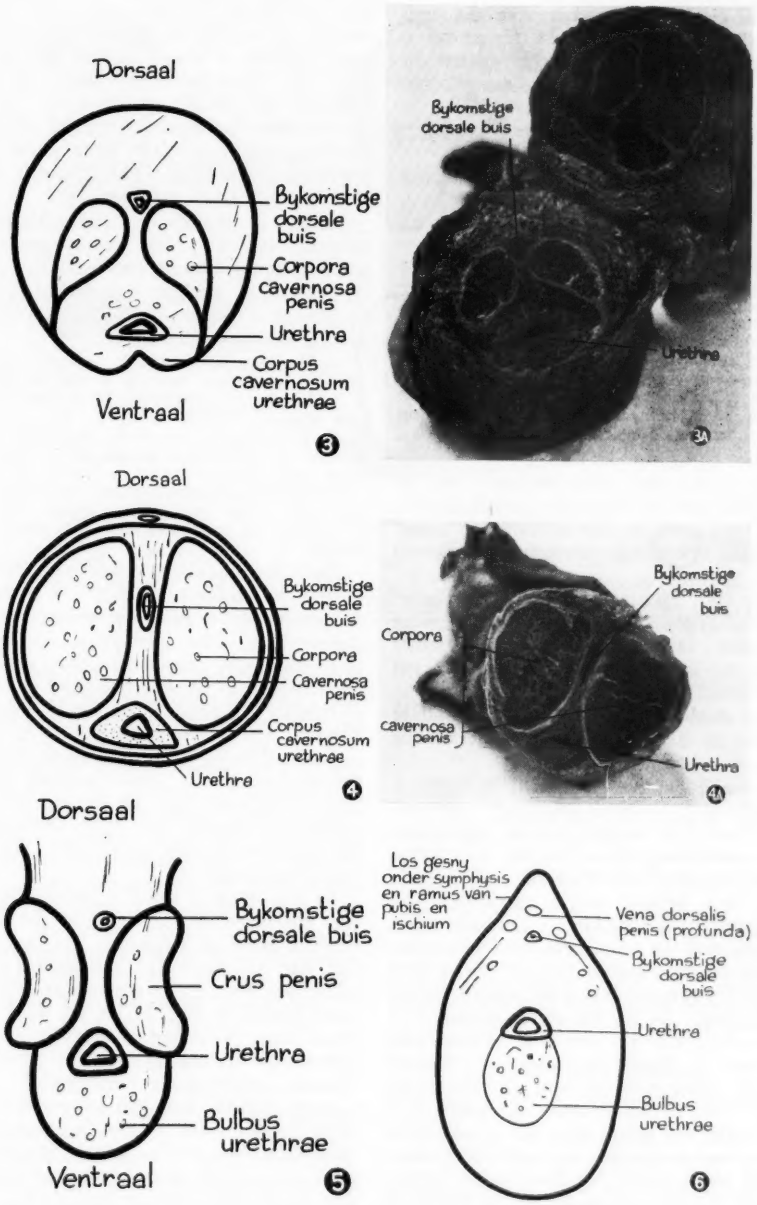


Fig. 3*A*. 'n Snit een duim agter die glans met die bykomstige buis dorsaal.

Fig. 4*A*. 'n Snit twee duim agter die punt van die glans. Die bykomstige dorsale urethra geleë tussen die corpora cavernosa.

dit kan op enige punt langs die dorsum voorkom, altyd in die middellyn. In meer as die helfte van die gevalle is daar voor die opening 'n geut soos in epispadie gesien word. Die lengte van die buis en wyse waarop dit eindig, varieer grootliks. In sekere van hierdie buise wat beskryf is, was daar 'n epiteel-voering van meerlagige plaveiselepiteel.

Chauvin[4] gee 'n klassifikasie van 5 aparte groepe:

(a) Duplikasie van die urethra van die glans tot by die blaas;
(b) Onvolledige duplikasie wat blind eindig en ventraal van die ware urethra open;
(c) Onvolledige duplikasie wat dorsaal van die ware urethra open;
(d) Y-vormige urethra, waar die bykomstige urethra in die ware urethra open distaal van die eksterne of interne sfinkter;
(e) Y-vormige urethra waar die bykomstige urethra by die wortel van die penis open en meer proksimaal by die normale urethra aansluit.

Hierdie tipe van klassifikasie is nie so duidelik as die van Nové-Josserand nie, en lê nie klem op die algemene dorsale ligging van die buis asook op die verwantskap tussen die dorsale bykomstige urethra en epispadie nie.

Slotkin en Mercer[5] kwoteer De Berne-Lagarde se gegewens dat daar tot 1932, slegs 38 gevalle van dubbele manlike urethra gerapporteer is. Sedertdien het daar van tyd tot tyd gevalle in die literatuur verskyn. 'n Volledige dubbele urethra is 'n veel seldsamer verskynsel as die van 'n bykomstige dorsale urethra.

Die teorieë om hierdie gevalle te verklaar, is veelvuldig. Nové-Josserand kwoteer teorieë, wat deur sekere persone gepostuleer is na aanleiding van gevalle. Luschka, Pribam, Verneuil en Picardat het hierdie dorsale buis beskou as 'n afvoerbuis van 'n bykomstige prostaatklier. Dit was egter slegs gegrond in die geval van Luschka, waar hierdie bykomstige buis in klierweefsel met die histologiese bou van prostaatweefsel geëindig het. In al die ander gevalle kon hierdie teorie nie die afwyking verklaar nie. d'Englisch en Taruffi se teorie, dat hierdie buis die afvoerbuis is van 'n abnormale uretrale klier, is nie gebaseer op enige feite nie. Lejars het gepostuleer dat hierdie buis ontstaan het as gevolg van onvolledige versmelting van corpora cavernosa, maar hierdie bewering is nie aanneemlik as 'n algemene verklaring nie. Die bou van die bykomstige buis en die verbindinge met die dieper dele van die urinêre-sisteem dui daarop dat dit werklik 'n bykomstige urethra is. Klers, volgens Nové-Josserand, het heeloorspronklik hierdie buis beskou as gevalle van epispadie wat vanself genees het weens die feit dat hierdie bykomstige buise wat op die dorsum open, dikwels 'n afwyking toon wat op epispadie lyk. Nové-Josserand kom tot die gevolgtrekking dat Delbet se opvatting die mees waarskynlike is om dorsale fistels of bykomstige urethrae te verklaar, naamlik dat hierdie afwyking die analoog is van epispadie wat net in 'n geringe graad voorkom.

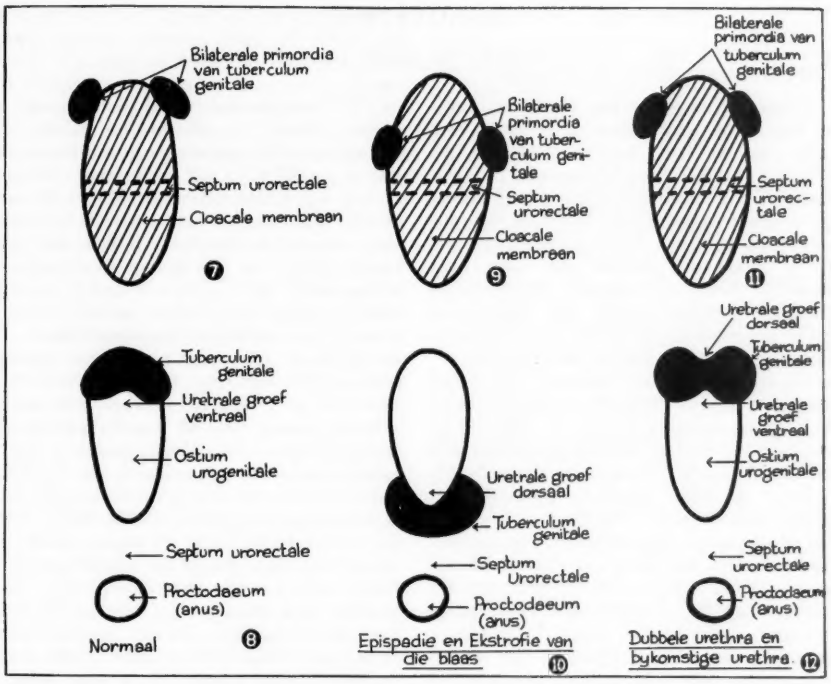
Patten[6] se beskrywing en verklaring van ekstrofie van die blaas en epispadie werp heelwat lig op hierdie probleem van dubbele en bykomstige urethrae wat dorsaal open. Sy opvattings in sake epispadie van die blaas kan as volg saamgevat word:

(a) Dat die oorspronklike gepaarde primordia van die tuberculum genitale te vêr koudaal geleë is, feitlik op die punt waar die septum urorectale gaan afgroei;
(b) Die corpora cavernosa ontwikkel dus net koudaal van die ostium urogenitale en die uretrale groef word gevorm dorsaal in plaas van ventraal;
(c) Gebrekkige ingroeiing van mesoderm en vinnige groei van die gebied tussen die ostium urogenitale en umbilicus laat die posisie verder versleg.

Deur hierdie uiteensetting van Patten toe te pas op dubbele urethrae en bykomstige dorsale urethrae kan gepostuleer word dat, indien: (a) die oorspronklike gepaarde primordia van die tuberculum genitale 'n klein bietjie te vêr koudaal geleë is; (b) daar 2 uretrale groewe sal ontstaan, ventraal en dorsaal. Die ventrale urethra sal die gewone pad van ontwikkeling volg, maar daar sal 'n bykomstige dorsale urethra volledig of onvolledig ontwikkel, met of sonder tekens van epispadie; daarom die groot verskeidenheid van wyses waarop die buise eindig, asook hulle variasie in lengte.

In Fig. 7 en 8 word 'n voorstelling gegee van die normale wyse waarop die urethrale ventrale groef totstandkom. Fig. 9 en 10 dui aan wat die moontlike agtergrond van epispadie sou wees en 'n soortgelyke voorstelling word gevind in Fig. 11 en 12, waar die ontstaan van 'n dubbele urethra of dorsale bykomstige urethra skematies uitgebeeld word. Hierdie embriolgiese agtergrond verklaar, waarom hierdie tipe van bykomstige urethra altyd dorsaal geleë is, met 'n opening in die middellyn en in 'n groot aantal gevalle geassosieer word met 'n uitwendige opening wat op 'n mate van epispadie dui. Dit is ook bekend, dat hierdie dubbele of bykomstige urethra deur gonorree aangetas word net soos die gewone urethra.

Die geval hierbo beskryf, sorteer dus onder



hierdie groep en is 'n dorsale bykomstige urethra wat betreklik volledig ontwikkel het, maar nie in die blaas open nie, en dus nie 'n funksionele tweede urethra is nie.

'n Bykomstige ventrale urethra of fistel van watter aard ookal, soos in die klassifikasies aangedui, moet volgens hierdie embriologiese beskouing 'n anomalie wees wat in verband staan met die ontwikkeling van die gewone ventrale urethra, net soos dit die geval is met hipospadie en behoort duidelik onderskei te word van 'n dorsale dubbele of bykomstige urethra wat sy agtergrond het in die abnormale embriologie en wat nie in die normale ontwikkeling van die urogenitalesisteem 'n plek het nie.

OPSOMMING

'n Geval van 'n dorsale bykomstige manlike urethra word beskryf.

Bestaande klassifikasies en moontlike teorieë van hierdie afwyking word bespreek.

Daar word gewys op die nouverwantskap tussen dubbele en bykomstige dorsale urethrae en epispadie.

Patten se verklaring van epispadie en ekstrofie van die blaas word in 'n gewysigde vorm toegepas as die mees waarskynlike verklaring van die afwyking.

SUMMARY

A case of accessory dorsal urethra in the male is described.

Current classification and theories about the pathogenesis are discussed.

The close relationship between double urethra and accessory dorsal urethrae and epispadias is demonstrated.

Patten's recent work on epispadias and extrophy of the bladder is applied in a modified form as the most probable explanation of this anomaly.

Dank is verskuldig aan dr. R. Campbell-Begg vir belangstelling en hulp met die Franse literatuur, asook aan prof. J. Barnetson vir die histologiese-snitte.

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ANNOTATION

HAEMOPHILIA

The disease haemophilia has fascinated clinicians for many years, but it is only very recently that we have begun to learn a lot more about it. We have commented in these columns[1] about recent advances in our knowledge of blood coagulation. Much of the progress in this field has been derived from the study of blood of patients who have bled abnormally. Some of these have been cases of classical haemophilia; others have differed in essential degree and this difference has been the starting point of further knowledge.

Recognition of classical haemophilia is not difficult. A familial bleeding disease, for practical purposes occurring only in males and transmitted by unaffected females, can be very little else. It is characterized by severe bleeding after minimal trauma, haemarthroses, bleeding from mucous membranes especially the genito-urinary tract, epistaxis, intramuscular haematomata and bleeding after tooth extraction. Blood loss is often of such severity as to threaten life. A prolonged whole blood coagulation time is the essential laboratory abnormality, since blood platelets, clot retraction, bleeding time and plasma prothrombin are all normal. The blood may take several hours to clot.

One of the first steps in the advance of our knowledge of the subject was the demonstration that the prothrombin was not adequately consumed during the clotting process.[2-4] This was followed shortly afterwards by the observation that the coagulation time need not necessarily be prolonged. Cases were described[5, 6] in whom it was shown that, even though the coagulation time was normal, prothrombin consumption was defective. Even more important was the fact that these patients' bloods were unable to shorten the coagulation time of classical haemophilic blood to the same degree as did normal blood. It was postulated, therefore, that these patients had the same defect but in milder degree.

It was while doing mixing experiments of this type that it was observed[7, 8] that occasionally one 'haemophilic' blood was able to fully correct a second apparently similar 'haemophilic' blood. This phenomenon resulted in the identification of 2 varieties of haemophilia, the first being called haemophilia and the second Christmas disease[9] (named after the surname of the first patient) or plasma thromboplastin component (PTC) deficiency.[10-12] The discovery of plasma (blood) thromboplastin[13] clarified the issue considerably. This is in part compounded of (*a*) platelets; (*b*) substances found in plasma or plasma after adsorption with alumina, e.g. antihaemophilic globulin (AHG); (*c*) substances found in serum, e.g. Christmas factor (CF). By means of this test it was very easy to demonstrate that classical haemophilia lacked the plasma factor (AHG) and Christmas disease lacked the serum factor (CF). Thus it has become possible to assay the amount of AHG and CF present in normal and abnormal blood. The principle of the AHG assay, for instance,[14] consists in comparing the amounts of thromboplastin generated by various dilutions of a standard normal and of the test plasma when factors other than AHG, necessary for the generation of thromboplastin, are supplied in optimal amounts. The standard normal plasma is considered to contain 100% AHG. With this method the range of plasma AHG concentrations in a group of normal people has been found to be from 50-220%. In 36 patients with haemophilia, values from 0-25% have been obtained. Fifteen patients suffered from mild haemophilia; their AHG concentrations ranged from 2-25% and when the figure exceeded 2% the coagulation time was likely to be normal. Less satisfactory (or more difficult) methods have been devised by others[15, 16] and a similar principle has been used for the estimation of CF.[17] The defect in any one family is usually constant in degree.[5, 6] It seems possible that with even more sensitive methods 'normal' people may be found whose content of plasma AHG approximates closely to the abnormal range.

The subject has become further complicated by the occurrence of other apparently similar deficiency states. It has been claimed[18] that a condition named plasma thromboplastin antecedent deficiency (PTA) can exist and is caused by the absence of another plasma substance; even a fourth[19] and a fifth[20] plasma thromboplastin component have been postulated.

Cases of multiple deficiencies in clotting factors have been described by Soulier and Larrieu[12] and Verstraete and Vandenbroucke[21] (AHG and CF), Koller[22] (AHG and factor 5 in each of 2 brothers), Bell and Alton[23] (CF and factor 7). In blood from 2 brothers Hill and Speer[24] showed by prothrombin consumption tests in the bleeding phase a combined defect of AHG and CF but in remission the defect in one brother was satisfactorily corrected by the addition of AHG alone. The

properties of PTA appear to be intermediate between or to summate those of AHG and CF and it is hard to resist the suggestion that PTA deficiency may really be a combined partial deficiency of both these factors.[25, 26]

All this might have been acceptable were it not for the persistent claims of Tocantins and his co-workers[27] that far from being a deficiency state, haemophilia is caused by an excess of 'anticephalin' in the blood. They were able to show that, contrary to the prevailing general impression, the coagulation of properly collected normal or haemophilic blood or plasma is accelerated when diluted with normal saline. It was claimed that stable plasma owed its fluidity *ex vivo* to the presence of inhibiting agents which lose much of their activity on dilution or contact with surface like glass. By appropriate dilution the rate of coagulation of haemophilic plasma could be made equal to that of normal plasma. These claims appear to have achieved spectacular confirmation by the demonstration[28] that the injection of haemophilic blood into normal recipients greatly increases the coagulation time of these recipients. It is not stated whether the haemophilics used had previously received blood or plasma transfusions —if so they may have developed a circulating anticoagulant—a not infrequent occurrence in haemophilia. If not—and if this work is substantiated—it will once again throw the field wide open and may be the precursor of even greater discoveries in the near future.

OPSOMMING

Die kennis van hemofilie het gedurende die afgelope paar jaar aansienlik toegeneem, en die maatstawwe waarvolgens 'n diagnose gedoen word, is tot in die fynste besonderhede uitgewerk.

Die tromboplastien-ontwikkelingstoets was 'n baie nuttige hulpmiddel by laboratoriumondersoek.

Dit het moontlik geword om die defekte in enige besondere familie te gradeer, om die verskillende soorte (bv. Christmas-siekte) te herken, en selfs om gemengde variëteite van die siekte te ontdek.

Die getuienis in verband met die patogenese van die siekte word ook kortliks bespreek.

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MITRAL VALVE SURGERY

ITS POST-OPERATIVE COURSE

M. M. ZION, M.B., B.CH. (RAND), M.R.C.P.
Johannesburg

Since the early publications on mitral valvotomy as a therapeutic measure in mitral stenosis,[1, 2] numerous reports on large numbers of cases have appeared in the literature. As stated by Goodwin *et al.*,[5] 'mitral valvotomy has now become a standard surgical procedure . . .'. The operative mortality is low, the average overall mortality being about 5%. The mortality is considerably lower in those patients not yet in the most advanced stages

of the disease (about 2%) and as, with the progress of time, it has become customary to operate on such less advanced cases, the risk of mitral valvotomy is now only slight.

Results have been good, with approximately 70% of patients obtaining a satisfactory result (improvement classed as *good* or *excellent*). There is impressive evidence that the operation confers a genuine and lasting benefit in the great majority of cases. Thus Ellis and Harken, in a follow-up of 6 months to 5 years, found that less than 9% of patients had regressed substantially after a definite improvement lasting 6 months or more.[4]

The close co-operation of surgeon and cardiologist in the pre- and post-operative phases has offered unique opportunities for study of the related problems. It is the object of this communication to discuss the early post-operative period, with its attendant complications and difficulties, and their management. While pure surgical complications related to thoracotomy are not within the scope of this paper, they are discussed when the presence of heart disease adds special problems of management.

MATERIAL

Eighty patients who were subjected to surgery of the mitral valve were personally seen by the author pre-operatively and daily post-operatively during their stay in hospital. The average stay in hospital after operation was 3 weeks. Three patients died during the operation or in the immediate post-operative period. The survivors were seen one month after discharge from the hospital and thereafter at monthly intervals for 3 months. There was a close liaison between the author and attending general practitioners and most complications seen by the latter were reported.

Uncomplicated Post-Operative Course. The patient returns to the ward, usually already conscious, though drowsy. A pericardial rub, often very transient, becomes audible in most cases. The intercostal drainage tube is removed in 24-48 hours. Fever may be present, but subsides in 2 or 3 days. The patient sits out of bed after 4-5 days, starts walking after 7-10 days, and at the end of 3 weeks is taking fairly long walks and may be climbing 2 flights of stairs. Cough is not troublesome and pain is not prominent after the first few days. After discharge from hospital, no untoward symptoms occur and in those in whom a satisfactory valvotomy was performed, a steady increase in effort tolerance is noted.

Shock. Surgical shock of sufficient severity to necessitate special treatment occurred in only 3 patients and was noted immediately on their return to the ward. In 2 patients the shock was associated with cerebral emboli while in the third, gross mitral regurgitation had been present and no surgical correction had been attempted. In 2 patients shock was treated by continuous intravenous infusion of noradrenaline (4 mg. per litre), the rate of the infusion being regulated to maintain systolic blood pressure above 100 mm. Hg. The third patient received 'Wyamine' (Wyeth) 30 mg. intravenously followed by 20 mg. intramuscularly 4-hourly. In 2 cases, shock was satisfactorily combated, but 1 of the patients subsequently died on the 5th post-operative day from the effects of cerebral embolism.

The patient with incompetence responded initially to noradrenaline but, 36 hours after operation, erythema marginatum appeared and 5 hours later he went into acute circulatory failure and died.

While surgical shock is thus not common following mitral valvotomy, its occurrence is usually associated with other complications. In itself, it can be satisfactorily treated with drugs which have a pressor action without any direct effect on the heart. Repeated plasma or blood transfusions and postural treatment, which are probably hazardous in cases of heart disease, are thus thought not to be necessary.

Pulmonary Atelectasis. Collapse of alveoli of varying degree occurs as a not infrequent complication of thoracotomy. Generally, the condition can be satisfactorily treated by physiotherapeutic measures, of which posturing is important. On the belief that, if a satisfactory valvotomy was performed, posturing would not be unduly hazardous it was permitted, with no untoward effects in any case. In those in whom no split or an unsatisfactory split was performed, posturing was avoided.

Purulent Bronchitis. This was not uncommon in patients with a previous history of recurrent bronchitis, but the vigorous use of breathing exercises and administration of the appropriate antibiotic usually resulted in rapid improvement.

Atrial Fibrillation. Of 38 patients in sinus rhythm pre-operatively, 18 (48%) developed atrial fibrillation in the immediate post-operative period. Four reverted spontaneously to sinus rhythm between the third and twelfth post-operative days. Of the remaining 14, 11 were converted to sinus rhythm with quinidine, while in 3 (8%) atrial fibrillation persisted despite intensive therapy with quinidine and procaine amide. Quinidine therapy was commenced on the twelfth to fourteenth post-operative days. The drug was given at 2-hourly intervals for 6 doses during each 24-

hour period and with each dose the patient took 2 drachms of aluminium hydroxide. The commencing dose was gr. 3, and every second or third day was increased by gr. 3 until either reversion to sinus rhythm occurred or toxic features (clinical or electrocardiographic) manifested themselves. Electrocardiograms were performed each day, 2 hours after the last dose of quinidine, and the drug was discontinued if evidence of toxicity, notably bundle branch block, appeared. In those patients in whom quinidine was successful, a maintenance dose of gr. 3 *t.d.s.* was given for 1 month.

Anti-coagulant drugs were not administered to cover the period of quinidine therapy, but no case of embolism occurred at the time of reversion to sinus rhythm.

As has been noted by other observers,[5, 8] prophylactic administration of quinidine did not reduce the risk of post-operative atrial fibrillation. The pre-operative administration of digitalis, on the other hand, did not increase the risk of atrial fibrillation and was regarded as advisable in that, if the arrhythmia set in, the ventricular rate was not unduly rapid. In 2 patients who had not received pre-operative digitalis, the onset of atrial fibrillation was accompanied by ventricular rates of over 200 per minute and the condition of the patients at the time gave rise to considerable anxiety.

POST-VALVOTOMY SYNDROME

Soloff and his co-workers first drew attention to a febrile syndrome following mitral valvotomy.[7] They regarded this as being due to rheumatic activity. Papp and Zion, reporting on 22 cases of a post-valvotomy syndrome, presented evidence against the syndrome's being due to active rheumatism and regarded it as a reaction to the presence of blood in the pericardium and pleura, the latter particularly if it was loculated.[6]

Sixteen patients in the present series manifested the syndrome and formed part of the larger series discussed by Papp and Zion.[6] The syndrome consists essentially of fever and left pleural effusion, with evidence of persistent pericarditis. Pain, not of incisional origin, is frequently present, but only occasionally severe. Such pain may be felt over the praecordial area or in the left side of the chest and is not related to respiration or posture.

The fever may occur early in the post-operative course, being continuous with that normally present for a few days, or it may commence anything up to 4 weeks post-operatively. It may last for a few days to several months, and a proportion of cases relapsed after 1-4 weeks. Several relapses, up to 4 years after operation, have been mentioned in the literature, but in the present series only one patient relapsed more than once, and the syndrome 'burnt itself out' in 6 months.

Clinical signs are few, consisting of the features of a left pleural effusion and, in occasional cases, a persistent pericardial friction rub. Electrocardiography often reveals diffuse T-wave inversions due to pericarditis. Radiography may reveal a left pleural effusion and enlargement of heart contour due to pericardial effusion.

The course of the illness is unaffected by treatment with antibiotics or salicylates and although it may be protracted, the outcome is always favourable and the results of valvotomy are not prejudiced.

The syndrome must be differentiated from true rheumatic activity (Table 1), pulmonary infarction and 'pneumonitis' (see below).

TABLE I: COMPARISON OF CERTAIN FEATURES IN THE POST-VALVOTOMY SYNDROME AND IN RHEUMATIC FEVER

	Post-Valvotomy Syndrome	*Rheumatic Fever*
Preceding Streptococcal Infection	Nil	Common
"Prophylactic Penicillin"	Ineffective	Often effective
Joint Pains	Nil	Common
"Myocarditis"	Nil	Common
Salicylate Response	Nil	Common
Prognosis	Good	Sometimes unfavourable
Raised E.S.R. and Muco-Proteins Presence of C-reactive Protein in Blood	Common	Common

Rheumatic Activity. Early in experience with mitral valvotomy it was feared that the operation would cause a flare-up of rheumatic activity which had been dormant. This fear was strengthened by the frequent finding of Aschoff nodes in excised atrial appendages. Happily, however, it has become apparent that the risk of precipitating rheumatic activity is very slight. It may be stressed that it remains a principle to delay operation, unless it be urgently indicated, in patients who have had

acute rheumatic fever within the preceding 5 years or in whom blood tests indicate subacute rheumatic activity.

Two patients in the present series developed clinical features of active rheumatism in the early post-operative period. The one (already referred to) developed erythema marginatum with a high fever 36 hours after operation, and died soon thereafter. Necropsy, however, revealed no evidence of Aschoff nodes in the myocardium. The second patient complained of joint pains and the electrocardiogram showed a prolonged P-R interval. There was no fever, but the E.S.R. varied between 16 and 24 mm. in 1 hour (Westergren). She was kept in bed, received salicylate therapy, and the signs of activity disappeared in 2 months. The outcome of her operation has been excellent (follow-up of 1 year).

There has been much controversy whether or not re-stenosis occurs after satisfactory splitting of the mitral valve. All are agreed, however, that further rheumatic activity presents a real danger that re-stenosis, or other valvular damage, may ensue. A patient who had had an excellent result from valvotomy performed in August 1950, developed acute rheumatic fever in January 1952. Two years later, effort dyspnoea re-appeared and progressed until, early in 1955, she was markedly disabled. Repeat operation revealed tight stenosis. A satisfactory split was again performed, with an excellent clinical result.

While it is clear that patients subjected to mitral valvotomy should receive antibiotics during upper respiratory infections or to cover dental extractions, there appears to be some justification for suggesting the use of continuous prophylactic penicillin for some years in all such subjects. Although the risk of rheumatic activity is small, its effects may be serious.

Pulmonary Infarction. Four patients had pulmonary infarction, presenting between the seventh and tenth days post-operatively. In 2 there was evidence of phlebothrombosis in the calf, but the source of clot in the other 2 could not be determined. Only one of the 4 had had a history of pre-operative pulmonary infarction. In no case was there much disability during the episode, and repeated infarctions did not occur. All 4 were treated with phenyl-indanedione ('Dindevan'), to maintain a prothrombin index between 40 and 50%, until their discharge from hospital.

Pulmonary Infections. Two patients had attacks of a febrile illness, with clinical and radiological features of pneumonitis, 6 and 8 weeks after operation. These are not included amongst the 'post-valvotomy syndrome' cases and both responded rapidly to antibiotics. It is, of course, possible that pneumonitis occurs in the lung underlying the left pleural effusion in patients with the post-valvotomy syndrome, but the course of the illness is quite different from that in the 2 patients here described. It is interesting to report that a patient who had had the post-valvotomy syndrome was 2 years later subjected to repeat operation for the treatment of aortic stenosis and at this operation part of the left lower lobe appeared almost carnified; unfortunately, no biopsy was taken.

Mental Disturbances. Wood mentioned psychosis in 5% of his cases in the immediate post-operative course, unexplained by cerebral embolism.[8] In the present series, a confusional state developed in one patient 3 days post-operatively and was followed within a few hours by slight left hemiparesis, suggesting that it was due to cerebral embolism.

A second patient, with no evidence of cerebral embolism, was completely disorientated for place and time for 1 week post-operatively, but recovered completely. In many cases, mild confusion was caused by pethidene given for relief of pain.

Several patients experienced depression post-operatively, but this was regarded as a symptom common to most major surgical procedures. In those patients with a good result, the depression rapidly disappeared when they discovered their 'new' effort tolerance.

Congestive Heart Failure. Some degree of congestive heart failure occurred in 11 patients, but this rapidly cleared on routine therapy. Its occurrence was not related to the presence of the post-valvotomy syndrome or to the quality of the split performed. It did not prevent a good result.

Pulmonary Oedema. Two patients developed acute pulmonary oedema within a few hours of operation. Both had had combined stenosis and incompetence and, in both, limited splits of the anterior commissure had been performed. The attacks were satisfactorily treated with venous cuffing of the limbs, sedation, oxygen administration, intravenous aminophylline and continuation of the digitalis and mercurial therapy which they had been receiving.

Systemic Embolism. Four patients had a total of 5 systemic emboli at the time of, or shortly after, operation. There were 3 cerebral emboli, and 2 to the lower limbs. One patient with a cerebral embolus died from the

effects of the embolus. While the incidence of systemic embolism is low (5% in the present series; 8% in Ellis and Harken's series[4]; 10% in Wood's series[8]; 6% in Belcher and Somerville's series[3]), its effects may be disastrous. Thus, Belcher and Somerville record a mortality of 45% in their patients with cerebral embolism, and mention a mortality of 66% according to Bailey.[3]

A large proportion of the patients comprising the present series formed the more recent cases in the series of Belcher and Somerville.[3] In these cases, surgical manoeuvres to lessen the risks of embolism and to attempt to deviate any dislodged clot away from the cerebral circulation, were performed as described by Belcher and Somerville.[3] This may explain the somewhat lower incidence of operative systemic embolism in the present series, compared with that in the other reports. Nevertheless, the risk remains a real one, sometimes with tragic consequences.

As systemic embolism appears to arise from freshly formed clot,[3] it would seem that the use of anti-coagulants in the pre-operative period in those subjects particularly prone to embolism might be beneficial. With this in mind, a controlled study was commenced in which alternate patients with atrial fibrillation received a course of anti-coagulants for 2 weeks pre-operatively. For 10 days they received Dindevan to maintain a prothrombin index of 40-50%; for the next 4 days they received heparin, to maintain a clotting time approximately double normal. The last dose of heparin was given intravenously 12 hours before operation. If the clotting time was not normal just before operation, protamine sulphate 100 mg. was given intravenously. There are insufficient cases to draw any definite conclusions and the study is continuing. Preliminary impressions are encouraging.

COMMENT

Mitral valvotomy constitutes one of the greatest advances in cardiac surgery; the risk of operation is small and the results well worth while. However, during the first few post-operative weeks the patients not infrequently experience complications which make the morbidity of the operation high. The most serious complication (systemic embolism) is rare and the next most serious (rheumatic activity) rarer still.

Many patients develop one or other of the complications discussed, following their discharge from hospital. The practitioner who is confronted with such cases may often be at a loss to explain them. However, in the light of general experience, the complications have been found to fall into definite categories, few of which are serious. Of greatest importance to the practitioner is the post-valvotomy syndrome, with which he will not infrequently be confronted. A knowledge of the benign, though protracted, course of the illness enables him to manage these cases with confidence and to give the patient the very necessary reassurance about the eventual favourable outcome.

In view of the doubt about the frequency of re-stenosis, all patients subjected to mitral valvotomy need to be watched at regular intervals for many years, so that the true incidence of re-stenosis can be ascertained and so that the patients concerned may be offered the benefit of a second operation, if necessary.

SUMMARY

Eighty patients subjected to mitral valve surgery were closely watched in the post-operative period. They were found to be liable to many complications which made the morbidity high, but very few of the complications were serious or unfavourably affected the outcome of the operation.

OPSOMMING

Tagtig pasiënte wat myterklep-chirurgie ondergaan het, is sorgvuldig gedurende die na-operasietydperk dopgehou.

Daar is bevind dat hulle vatbaar was vir talle komplikasies wat die morbiditeit verhoog het. Baie min van hierdie komplikasies was egter ernstig, of het 'n ongustige uitwerking op die gevolge van die operasie gehad.

The patients in this series were studied by the author during the tenure of his post as Cardiological Registrar to the London Chest Hospital and he expresses his gratitude to the physicians and surgeons on the staff of the hospital for allowing him to have access to their patients.

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PRIMARY PERITONITIS*

WILFRED KARK, F.R.C.S.

Department of Surgery, University of the Witwatersrand, Johannesburg

Primary peritonitis is mainly a disease of children. About 3 out of every 4 cases occur under the age of 5 years. It is one of the conditions which must be considered in the differential diagnosis of the acute abdomen, particularly as opposed to secondary peritonitis, which most commonly arises as a sequel to acute appendicitis. It is especially during the early years of life, when the clinical story and the subjective evidence are not yet clear and precise, that the diagnostic problem is greatest. This problem has practical implications in that a diffuse primary peritonitis is amenable to chemo- and antibiotic therapy, whereas secondary peritonitis requires laparotomy and definitive treatment of the primary cause.

In order to elucidate various aspects of this problem, a series of cases admitted to the Transvaal Memorial Hospital for Children over a period of 5 years was reviewed.

CLINICAL MATERIAL

All cases diagnosed as primary peritonitis during this 5-year period were included in the review; they total 36. The case notes were analysed and, despite a considerable and not unexpected variation in the detail recorded, it was found possible to abstract sufficient data to justify certain conclusions. It should be stated at once that such a method of evaluation (i.e. solely from the recorded notes on the case) is subject to the reservation that in some instances all the findings and impressions of the several medical attendants in any one case may not have been entered. However, it is presumed that the features crucial to the final diagnosis were not omitted from the records.

Table I presents the clinical features of the series.

DIAGNOSIS BASED UPON OPERATIVE FINDINGS

The first 11 cases in Table I are those whose diagnosis was based upon the findings at operation. In no less than 9 cases the pre-operative diagnosis was acute appendicitis and this label was changed at operation to primary peritonitis. The reasons for this diagnosis at operation were the 'normal' appearance of the appendix in 5 cases and, in the remaining 6 cases, the observation that, despite evidence of a pathological appendix, the degree of the peritonitis appeared to be disproportionately excessive. Of the first 5 cases, one is recorded as exhibiting free, glairy fluid which was negative on culture, and the other 4 have records of a generalized peritonitis, with non-odorous pus in 3 of them, and positive pneumococcal cultures in two. In the second group of 6 cases exhibiting some appendiceal affection, there are records of 2 with diffuse peritonitis; in one of these 6 there was a positive culture of non-haemolytic streptococci, and negative cultures are reported in 4 cases.

On the criterion of the finding of a diffuse peritonitis, 6 of the 11 in this group may be considered as probable cases of primary peritonitis. In the other 5, this evidence is equivocal, and when the clinical features are added to the assessment, the diagnosis would seem to have been more likely a secondary peritonitis or a non-infective peritoneal reaction to some primary condition in an abdominal viscus.

DIAGNOSIS BASED UPON ASPIRATION

The next 4 cases listed in Table I were diagnosed after abdominal paracentesis. In 3, the immediate examination of a smear of the aspirated fluid showed gram-positive cocci. In 2 of these the pus is noted as being non-odorous; in 1, a culture yielded non-haemolytic streptococci, in another the culture was negative, and in the third there is no record of the findings on culture. In the fourth case (with localizing symptoms and signs) paracentesis did not produce any peritoneal fluid.

Primary peritonitis in the first 3 of this series seems a possible and acceptable diagnosis, but in the fourth case the clinical picture and the negative result of aspiration point to another cause.

DIAGNOSIS BASED ON CLINICAL PICTURE

In the remaining 21 cases the diagnosis was based upon criteria other than operative findings and paracentesis.

An analysis of the recorded findings in regard to the localization of *pain, tenderness* and *rigidity* in this third group brings out the features tabulated in Table II.

The remarkable findings in this analysis are:

(a) Generalized pain, the expected symptom of primary peritonitis in children, is recorded in only 4 cases.

(b) In as many as 4 cases (and there was 1

* This paper is based upon a communication to the Southern Transvaal Group of the Association of Surgeons of South Africa.

TABLE 1

Case	Respiratory Infection	Vulvo-Vaginitis	Diarrhoea	Vomiting	Abdominal Pains	Abdominal Tenderness	Abdominal Rigidity	Abdominal Distension	Borborygmi	General Condition
1. B.M.	Tonsillitis	—	—	+++	General continuous	General ..	General ..	—	Absent	Fair
2. A.G.L.	—	+	—	+	General	General especially right iliac fossa	General ..	+		Good
3. M.C.M.	—	—	+	+	General	General ..	General ..	—		Looks ill
4. E.K.P.	—	Slight ..	+	++	General	General ..	General ..			Looks ill
5. K.B.	—	—	—	—	General	No record ..	No record ..			Looks well
6. M.J.B.	—	Discharge +	—	++	Lower abdominal	Lower abdomen	Lower abdomen			Ill
7. G.B.	—	Discharge +	—	+++	Right iliac fossa	Right iliac fossa	Right iliac fossa			Looks well
8. A.B.	+	—	—	+	Right iliac fossa	Right half ..	Right rectus ..			Looks well
9. O.S.	—	—			Generalized intermittent	Right iliac fossa	General, especially right iliac fossa	+		Looks ill
10. R.E.K.	—	Discharge +	+	+	Began centrally, later in right iliac fossa	Right iliac fossa	Right iliac fossa			Looks ill
11. B.G.			+++ (5 days)	+++ (6 days)	General for 1 day	General ..	Absent	+	+	Looks ill
12. A.H.	—	—	+	+++	General	General ..	General ..	—	Absent	Good
13. E.L.	—	—	+	++	General	General ..	General ..	Slight		Ill
14. H.O.F.	—	Discharge +	—	++	General	General ..	General ..		Absent	
15. P.R.	—	Vulva red	—	++	Began generally, later in right iliac fossa	Lower abdomen	General ..		Faint +	Ill and in pain
16. F.S.	+	Discharge +	—	+	General especially in right iliac fossa	Right iliac fossa	Absent	—	+	Good
17. A.D.D.	—	Discharge +	—	+	Right iliac fossa	Both iliac fossae	Absent ..		+	Good
18. E.G.W.	—	Discharge ++	+	++	Began centrally, later in right iliac fossa	Right iliac fossa	Absent ..	—	+	Good
19. A.v.R.	—	Discharge ++	—	—	Began in right iliac fossa, later in lower abdomen	Both iliac fossae	Absent ..	—	+	Good
20. H.A.	—	Slight discharge	—	++	Began centrally, later in left iliac fossa	General, mainly left iliac fossa	General ..	Slight		Ill
21. P.E.B.	+	Discharge +	++	+	General	Right iliac fossa	Right iliac fossa			Ill
22. M.F.	+	Discharge ++			Began centrally, later in right iliac fossa	Right iliac fossa	Right iliac fossa			Ill
23. N.M.	—	Discharge ++	+++		Lower abdomen	General ..	General ..	+		Very ill
24. N.M.		Slight discharge	+		Right iliac fossa	Right iliac fossa				Ill
25. J.W.		Discharge ++	—	+++	Right iliac fossa	Right iliac fossa	Right rectus ..			
26. R.M.		Slight discharge	—	+	Lower abdomen	Both iliac fossae	Right rectus ..	+		
27. L.B.	+	Slight discharge			Central	Both iliac fossae	Both iliac fossae			Looks well
28. A.K.			++	++	Lower abdomen					Looks well
29. C.Mc.D.		Slight discharge		+	General	General ..	Absent			Looks ill
30. R.H.		Discharge ++			General					
31. S.J.H.		Discharge ++		Only nausea	Central	Both iliac fossae	Both iliac fossae			Good
32. R.R.			+++							Very ill
33. M.B.	—	Discharge ++	—	—	Right iliac fossa	Right iliac fossa	Lower abdomen			
34. Y.V.	—	Discharge ++	—	—	Began centrally, later in right iliac fossa	General ..	General ..			Not ill
35. H.S.		Discharge +	—	+	Began generally, later in right iliac fossa	Right iliac fossa	Absent			Looks well
36. M.P.		Discharge +	+	++	Upper abdomen	Both iliac fossae	Right iliac fossa			

— = Negative; + = Positive.

TABLE II: LOCALIZATION OF PAIN, TENDERNESS AND RIGIDITY IN THE THIRD GROUP OF CASES
(The figures given in brackets are the corresponding findings abstracted from Groups 1 and 2).

	Diffuse	*Lower Abdomen*	*Central to Right Iliac Fossa*	*Right Iliac Fossa*	*Central*	*Upper Abdomen*
Pain	4 (9)	4 (1)	4 (2)	5 (2)	2	1
Tenderness ..	3 (8)	6 (2)		8 (4)		
Rigidity.. ..	2 (8)	3 (1)		5 (4)		

from each of the other 2 series as well) the pain began generally or centrally and later settled in the right iliac fossa.

(c) In a further 5 (plus 2 from the other groups), the pain began and remained in the right iliac fossa.

(d) In the remaining 7, where there was a record of abdominal pain, it had some other localization.

(e) The findings as regards tenderness and rigidity are comparable and even more remarkable. A localized tenderness was described nearly 5 times as often as diffuse tenderness; and limited rigidity figures 4 times more often than the generalized state.

An analysis of diarrhoea and vomiting in this series does not reveal anything of significance relating to the underlying reason for the diagnosis. Repeated vomiting is a recognized feature of primary peritonitis; it is recorded in less than one-fifth of these cases. The incidence of diarrhoea is also low.

The notes on abdominal distension and borborygmi are too sparing to throw light on diagnostic criteria; and the information culled from the temperature charts and the blood counts are also of little help in assessing what features were used in deciding the differential diagnosis.

The notes under the heading of 'General Condition' are of interest. In primary peritonitis an early deterioration of the general condition is to be expected; only one-third of the 21 cases in this series bears such a record.

Up to this point in the analysis of the clinical picture, a very small number, amounting to about 1 in 5 cases, can be said to present a reasonable foundation for the diagnosis of primary peritonitis; and it appears that there must necessarily be some exceptional reason for this diagnosis in the face of so much contrary evidence. From the records it is apparent that the 'exceptional reason' comes under the heading of 'vulvo-vaginitis': a vaginal discharge is noted in 19 cases. In 7 of these an immediate smear revealed Gram-positive cocci. The findings on culture of a vaginal swab are as follows:

Staphylococcus albus	2
Staphyloccocci and diphtheroid bacilli	4
Staphylococcus aureus	1
Coliform and diphtheroids	3
Haemolytic streptococci	1
Non-haemolytic streptococci	2

These culture results, apart from the one haemolytic streptococcus, are not significant in the diagnosis of primary peritonitis, since there is general and authoritative support for the fact that primary peritonitis in children is caused by a haemolytic streptococcus or by a pneumococcus in most cases, and by coliform bacilli and other organisms in the remaining small proportion. It therefore appears that it was the presence of a vaginal discharge that was judged to be the crucial feature leading to the diagnosis of primary peritonitis in the great majority of this last group of cases.

It is important to note that the laboratory report on the result of examination of the vaginal swab was often delayed for 5-9 days, and usually this report was delivered after the patient had recovered from the acute abdominal state and, in some cases, after discharge from hospital.

The culture results suggest the high degree of error in a diagnosis based on this criterion, and the review of the clinical features shows how unwarranted and misleading is the use of this feature in diagnosis. There is, moreover, a considerable body of opinion and evidence against the assumption that vaginal infection is a cause of primary peritonitis. Since this review was begun, routine examination of a series of consecutive admissions has shown that a degree of vaginal discharge is not at all uncommon in little girls, and that the most common source of this is a vulvitis. Gross,[1] in discussing the female genital tract as a path of invasion of the peritoneum says:

'This theory, of course, utterly fails to explain the mode of infection in males. It is our belief that invasion by way of the uterus occurs but rarely because autopsy examination in our fatal female cases has never shown evidence of ascending genital tract infection'.

SUMMARY AND CONCLUSIONS

Thirty-six cases diagnosed as 'primary peritonitis' are reviewed.

In the first group, where diagnosis is based upon operative findings, 9 out of 11 were preoperatively diagnosed as appendicitis; and only 6 had possible and acceptable evidence leading to a final diagnosis of primary peritonitis.

In the second, where paracentesis of the peritoneal cavity was done, 3 out of the 4 cases had reasonably definite evidence of a primary peritonitis.

In the third group, the margin of error in the diagnosis is considerable, and it seems very likely that, in at least two-thirds, the diagnosis of primary peritonitis can be ruled out with certainty, and that in over four-fifths of the cases the diagnosis was probably incorrect. The misleading feature in this group was the finding of vulvo-vaginitis. The obvious inference to be drawn from the analysis in this group is the strong likelihood that the proper diagnosis in most instances was in fact a secondary peritonitis.

Because of such a high degree of error it is justifiable to generalize that it is safer to do a laparotomy as a routine when the diagnosis of peritonitis is made. If it be found to be primary, little or no harm is done by closing the laparotomy and treating with the proper antibiotics; if it be found to be secondary, then a satisfactory definitive procedure (in most cases appendicectomy) can be performed. On the other hand, it is clear that there is considerable risk if an acute appendicitis complicated by peritonitis is left without operation because of an error in diagnosis.

OPSOMMING

Ses-en-dertig gevalle wat as ‚primêre buikvliesontsteking' gediagnoseer is, word in oënskou geneem.

In die eerste groep, waar die diagnose op operatiewe bevindings gebaseer is, is 9 uit 11 voor die operasie as blindedermontsteking gediagnoseer; in slegs 6 gevalle was daar moontlike en aanneemlike getuienis wat uitgeloop het op die finale diagnose as primêre buikvliesontsteking.

In die tweede groep waar 'n tapping van die buikvliesholte uitgevoer is, is redelik definitiewe bewyse van primêre buikvliesontsteking in 3 uit 4 gevalle aangetref.

In die derde groep was die vergissingsyfer in die diagnose aansienlik, maar dit lyk waarskynlik dat, in ten minste twee-derdes van die gevalle, die diagnose van primêre buikvliesontsteking met sekerheid buite beskouing gelaat kan word, en dat in meer as vier-vyfdes van die gevalle die diagnose waarskynlik verkeerd was. Die misleidende kenmerk in hierdie groep was die vulvovaginitis-bevinding. Die klaarblyklike gevolgtrekking wat gemaak kan word uit die ontleding in hierdie groep is die sterk waarskynlikheid dat die korrekte diagnose in die meeste gevalle inderdaad sekondêre buikvliesontsteking was.

Weens die hoë mate van vergissing is dit geregverdig om tot die algemene gevolgtrekking te geraak dat dit veel veiliger is om 'n laparotomie as roetine-behandeling uit te voer wanneer 'n diagnose van buikvliesontsteking gedoen word. As daar bevind word dat dit primêr is, word min of geen skade aangerig as die laparotomie toegewerk en die pasiënt met die regte antibiotica behandel word nie; as daar daarenteë bevind word dat dit sekondêr is, kan 'n bevredigende definitiewe prosedure (in die meeste gevalle 'n appendisektomie) uitgevoer word. Aan die ander kant is dit duidelik dat daar aansienlike risiko's is indien akute blindedermontsteking, deur buikvliesontsteking gekompliseer, nie geopereer word ten gevolge van die verkeerde diagnose nie.

It is a pleasure to express my thanks to Dr. K. Mills, Superintendent of the Johannesburg Hospital, for permitting me to have access to the records.

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TOXICITY OF SOME SOUTH AFRICAN SNAKE VENOMS

THEIR RELATION TO THE ACETYLCHOLINESTERASE CONTENT*

J. DE BOER, M.D.

Department of Physiology, University of Pretoria, Pretoria

In 1939 it was suggested[1] that acetylcholinesterase played a role in the curariform paralysis caused by snake venoms. The explanation offered seemed quite logical, viz. that destruction of acetylcholine would deprive the neuro-muscular junction of its means of impulse transmission.

In the light of our present conception of the function of acetylcholine and acetylcholinesterase in the process of chemical transmission

* The experimental work reported here was carried out in the Department of Pharmacology and Therapeutics of the University of the Witwatersrand Medical School, Johannesburg.

of nerve impulses, the foregoing suggestion is less acceptable. Since at a neuro-muscular junction acetylcholinesterase may exceed the required amount by 10-12 times,[2] is difficult to see how a small amount of acetylcholinesterase, free in the circulation, could exert such a profound influence.

There are definite indications, however, that the system acetylcholine—acetylcholinesterase may have an influence on the permeability of cell membranes.[2] It is interesting, therefore, to study the relations between the toxicity of snake venoms and their acetylcholinesterase content. It should be kept in mind, however, that even if no relation exists this need not invalidate the influence on the permeability of the cell membrane.

The unit of toxicity was defined as the weight of dried snake venom in grammes necessary to kill 1 gramme of mouse (by intraperitoneal or subcutaneous injection) within 24 hours, or the minimum lethal dose divided by body weight. Mature mice, with a body weight of 20-25 g. were fasted for 16 hours before the assay to reduce the weight of contents in the gastro-intestinal tract. The dose of the venom was adjusted according to the body weight. Mortality rate of the animals at the unit of toxicity level was 100%. A 5% decrease in dose caused a definite reduction in mortality.

The order of toxicity obtained with 6 different snake venoms are shown in Table 1.

TABLE 1

Dendroaspis polylepis	1 x 10^{-8} g,
Naja naja (Java)	5 x 10^{-7} g.
Haemachetes haemachetes	1 x 10^{-6} g.
Naja nivea (II)	6 x 10^{-6} g.*
Naja nivea (I)	8.5 x 10^{-6} g.*
Naja nigricollis	1 x 10^{-5} g.

*Roman ciphers indicate different batches from the same species.

The acetylcholinesterase activity of the venoms was determined titrimetrically as follows:

To 14 ml. distilled water were added 5 ml. acetylcholine solution 0.01 M. The temperature was kept constant at 20° C. After a predetermined time the hydrolysis was stopped by the addition of 1 ml. physostigmine salicylate solution 1%. The amount of acetic acid liberated was determined with the help of sodium hydroxide solution 0.0095 N, using phenolphthaleine as indicator. Controls established that no hydrolysis of acetylcholine occurred during ½ hour in the presence of physostigmine + snake venom. A second control was run for spontaneous hydrolysis of the acetylcholine in the absence of snake venom and physostigmine. All fluids had been brought as near as possible to neutral.

The enzymatic hydrolysis was allowed to proceed for 5, 10, 15 and 20 minutes. Every determination was done 4 times and the average of the figures obtained was taken as the final result.

Table 2 shows the results obtained with *Naja nivea* (*I*) venom, expressed in per cent acetylcholine hydrolysed.

TABLE 2

Time in minutes	*Hydrolysis (%)*
5	17.1
10	25.3
15	31.7
20	38.0

The influence of temperature on the reaction is shown in Table 3, the hydrolysis being stopped after 10 minutes:

TABLE 3

Temperature	*Hydrolysis (%)*
30° C.	18.2
40° C.	22.2
50° C.	24.2
55° C.	27.5
60° C.	18.5
65° C.	11.6
70° C.	4.4
75° C.	0

For the comparative acetylcholinesterase activity of the different snake venoms a 0.02 M solution of acetylcholine was used. The hydrolysis was allowed to proceed at 55° C. for various periods. The average of 4 determinations are shown in Table 4.

TABLE 4

Species of Snake (In Order of Toxicity)	*Hydrolysis % at 55° C. after Varying Periods*			
	5 Minutes	*10 Minutes*	*15 Minutes*	*20 Minutes*
Dendroaspis polylepis	2.4	4.5	6.2	7.9
Naja naja (Java)	5.5	9.2	11.7	14.2
Haemachetes haemachetes	23.8	30.8	45.8	49.3
Naja nivea (II)	33.7	57.7	80.2	91.3
Naja nigricollis	2.3	4.1	5.6	7.2
Control	1.5	3.2	5.0	5.5

Table 4 indicates that the strongest enzyme activity is shown by *Naja nivea* (*II*) and that the greatest toxicity is found in the venom of *Dendroaspis polylepis* and *Naja naja*.

The hydrolytic index is derived from the following formula:

$$x = k\ (H\text{-}h) : T$$

where x is the hydrolytic index, k is a constant (10^{-6}), H is hydrolysis %, and h is hydrolysis % in the control; T is the unit of toxicity.

The results in order of toxicity are shown in Table 5.

TABLE 5

Dendroaspis polylepis	4.8
Naja naja (Java)	17.4
Haemachetes haemachetes	43.8
Naja nivea (*II*)	14.3
Naja nigricollis	0.17

These calculations show that toxicity does not coincide with the acetylcholinesterase activity.

The problem has also been studied in rats and mice, a comparison being made between 2 venom solutions. One solution had been subjected to a temperature of 75° C. for 10 minutes, whereas the other solution, not heated before use, served as control. The inactivated venom solution did not show any acetylcholinesterase activity after cooling to room temperature. For this experiment venom of *Naja nivea* (*II*) was used with a hydrolytic index of 14.3 and a unit of toxicity of 6×10^{-6} g. The dose injected was 10 units per g. body weight. In this case the unit of toxicity was for rats and mice the same. Twenty-four rats and 48 mice were used, half the number in each group being controls. No essential difference in survival time (time between injection and death) was observed in the 2 groups.

It is obvious from the determinations of the units of toxicity and the acetycholinesterase activity that there does not exist any relation between these properties in the 5 venoms compared. This fact seems in accordance with the finding that there is no important change in survival time of animals injected with 10 times the minimal lethal dose.

SUMMARY

1. The toxicity of 6 different snake venoms is expressed in units.

2. The acetylcholinesterase activity of these venoms was determined titrimetrically. The hydrolytic index of the venoms was calculated.

3. By comparing the toxicity of the venoms with their hydrolytic index it was demonstrated that acetylcholinesterase cannot play a role in the toxicity of the venoms.

4. This fact is furthermore demonstrated by the absence of significant change in survival time with venoms containing inactivated acetylcholinesterase.

OPSOMMING

1. Die toksisiteit van 6 verskillende soorte slanggif word in eenhede uitgedruk.

2. Die asetielcholienesterase-aktiwiteit van hierdie gifsoorte word titrimetries vasgestel. Die hidrolitiese aanwysingsnommer van die gifsoorte is bereken.

3. Deur die toksisiteit van die vergifte met hul hidrolitiese aanwysingsnommer te vergelyk, is daar aangetoon dat asetielcholienesterase geen rol in die toksisiteit van die gifsoorte kan speel nie.

4. Hierdie feit word ook gedemonstreer deur die afwesigheid van enige betekenisvolle verandering in oorlewingstyd met gifsoorte wat ongeaktiveerde asetielcholienesterase bevat.

The expenses of this work were defrayed by a grant from the Council for Scientific and Industrial Research, Pretoria.

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2. Nachmansohn, D. (1950): *Chemical Control in Nervous Activity* in *The Hormones II*, 516, by Pincus, G. and Thimann, K. V.

NOTES AND NEWS · BERIGTE

Joan Griffiths (nee Cox), M.B., B.Ch. (Rand), D.C.H. (R.C.P. & S., Eng.) has commenced practice as a paediatrician at 209 Rosebank Galleries, Rosebank, Johannesburg. (Telephones:— *Rooms*: 42-2576; *Residence*: 41-5260), and at 36 Moray House, Jeppe Street, Johannesburg. (Telephones:— *Rooms*: 22-1351; *Emergency*: 22-4191.)

NAPT COMMONWEALTH FELLOWSHIP 1957

A Fellowship of £350 to enable a medical graduate from the Commonwealth to spend 3 months in the United Kingdom in the post-graduate study of tuberculosis, is offered by the National Association for the Prevention of Tuberculosis.

The intention of the award is to provide training and experience for a doctor who will subsequently play his part in the control of tuberculosis in his own country, the period of study leave to be at least 3 months in the United Kingdom. It is hoped the successful candidate will arrive in the United Kingdom by the end of March 1957.

Full particulars may be obtained from the National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1. The closing date for receiving applications is 30 November 1956.

THE TRANSVAAL CARDIAC SOCIETY

The first meeting of this Society was held on 12 September 1956 in Johannesburg. The following papers were read:

The Electrocardiogram in Hyper- and Hypo-Calcaemia (Dr. B. Bradlow).

Broncho-Pulmonary Sequestration (Dr. C. G. Caro).

Electrocardiographic Case Presentations (Dr. B. van Lingen and Dr. M. Zion).

Two Radiological Case Presentations (Mr. D. Adler and Dr. J. Meyer).

Interesting Cases (Presented by Members).

CAN YOU QUALIFY FOR THE CORONARY CLUB?

BUSINESS HAS BEEN ADVISED TO PROTECT ITS EXECUTIVES FROM OVERWORK

This advice from Francis J. Curtis, Vice-President of the Monsanto Chemical Company, was reported recently by Robert K. Plumb in the *New York Times*. Mr. Curtis indicated that the attitude of business toward its executives should be the same as that for protection of any other valuable company property. He pointed out that a man 47 years old, who had started his business career at 22 at a salary of $3,600 and had advanced to the echelon of top management at a salary of $40,000 was worth to the Company $425,000 at the very least.

In laying down membership requirements for the Coronary Club, he said that the most deceitful thought imaginable was the 'it can't happen here' point of view. For unbelievers he offered a set of rules running approximately as follows:

1. The job always comes first; personal considerations must necessarily be secondary.

2. Work done in the evenings, as well as on Saturdays, Sundays and holidays, is often the most effective of all.

3. Taking a brief-case home evenings provides an unrivalled opportunity to review (and relive) the troubles of the day.

4. Make it a point never to refuse a request—and always be ready to volunteer for additional responsibility.

5. Never neglect such auxiliary activities as banquets, meetings, speaking engagements and committee work.

6. Meal-times can be productive and it is well to plan conferences and business engagements around lunches and dinners.

7. Golf, gardening, sailing, fishing—any foolish recreation is wholly unprofitable and consequently a waste of time.

8. Be wary of taking too much vacation time—anything might happen while you are away.

9. Avoid delegating too much responsibility; and then keep a careful scrutiny over whatever has been delegated.

10. Do not waste time travelling. Plan your trip so that you can drive at night during the unproductive part of the day. You may go farther than you planned.

VIADRIL: A NEW STEROID ANAESTHETIC

A steroid, Viadril (21-hydroxypregnane-3:20-dione sodium succinate), has been used as an anaesthetic in 19 cases. Lerman discusses the pharmacology of the drug described and its mode of administration. Usually premedication was with omnopon and scopolamine, and maintenance by nitrous oxide and oxygen. In some cases relaxants were also given.

Viadril anaesthesia resembles normal sleep; relaxation is fairly good and bleeding usually much reduced. The patient is fully awake in an hour or so after operation, feeling well and without pain. Hormonal effects are absent and vomiting is rare.

Disadvantages are the slowness of induction and the risk of thrombophlebitis in the injected arm. Measures to combat these are suggested.

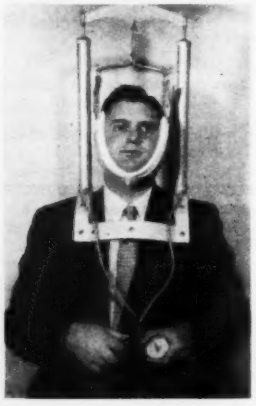
Details of the 19 cases are tabulated, and 3 cases are histories given to emphasize special points.

(Lerman, L. H. (1956): Brit. Med. J., **2**, 129).

PREPARATE EN TOESTELLE

DIE KUHLMANN SERVIKALE STREKKINGSAPPARAAT

Die Kuhlmann pneumatiese stel is 'n eenvoudige apparaat om servikale strekking toe te pas. Dit is lig in gewig, draagbaar en geskik vir gebruik in die spreekkamer, in die pasiënt se huis of in 'n verpleeginrigting. Dit is baie toepaslik en kan in enige houding gebruik word, d.w.s. sittende, lêende of selfs in 'n lopende posisie.



Die apparaat bestaan uit 'n gerieflike leer kopstuk wat verbind is aan 'n borsstuk wat pneumaties werk. Strekking word verkry deur die gomlastiekbal te druk op dieselfde manier as 'n Baumanometer. Dit veroorsaak 'n styging van die horisontale balk wat sodoende die kopstuk lig. 'n Drukmeter dui die presiese drukking in Kilogramme aan en 'n totaal van 25 Kg. (55 lb.) kan toegepas word.

Hierdie metode om strekking toe te pas is baie gemaklik en deurdat die pasiënt self die apparaat kan beheer en aansit, gee dit die nodige selfvertroue. In geval die drukking te veel is, kan die pasiënt dit onmiddellik self verlig.

Nog 'n voordeel van hierdie metode is dat daar 'n stadige, egalige strekking toegepas word, wat dit moontlik maak dat die pasiënt sy nekspiere natuurlik en aangenaam kan verslap. Wanneer die strekking verlig word, word dit stadig gedoen sodat die spierweefsel geleidelik verslap sonder om die verbindings-struktuur te skok.

U sal vind dat die Kuhlmann servikale strekkingsapparaat onoortreflik is in die behandeling van been- en gewrigsontsteking waarby senu-wortels betrokke is asook enige diskus beserings in hierdie gebied.

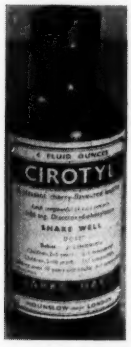
Die prys van die apparaat, kompleet, is £17 10s.

Enigste Verspreiders in Suidelike Afrika: Medical Distributors, Jeppestraat 236 (Posbus 3378), Johannesburg.

CIROTYL

Parke Davis Laboratories (Pty.) Limited, die Suid-Afrikaanse filiaalmaatskappy van Parke, Davis &

Company, kondig die beskikbaarstelling aan van Cirotyl, 'n lakserende preparaat bevattende diasetoksidifenielisatien, 'n sintetiese derivaat van difenielisatien, wat geïdentifiseer is as die aktiewe lakserende beginsel van Kalifornië-pruimedante.



Cirotyl word nie geabsorbeer nie; dit skyn asof dit sy effek uitoefen deur aanraking met die ingewandslymvlies, in teëstelling met samestellings soos antrachinoon en fenolftaleïen wat optree deur middel van kontak met die slymvlies sowel as deur absorpsie en her-afskeiding in die dikderm. Die effek van Cirotyl is sag maar standhoudend, en is soortgelyk aan die natuurlike bewegings van die ingewande.

Indikasies: Cirotyl word aangedui vir die voorkoming en behandeling van toevallige en kroniese hardlywigheid; dit is veral geskik vir die voorkoming van hardlywigheid tydens herstel- of behandelingsperiodes wat dieetkundige beperkings meebring.

Dosis en Toediening: Iedere teelepelvol (4 k.s.) Cirotyl bevat 1.66 mg. diasetoksidifenielisatien in 'n smaaklike draer.

Die volgende dosisse wat, indien nodig, binne 24 uur herhaal of op die volgende dag verdubbel kan word, word aanbeveel:

Suigelinge	¼- tot ½-teelepelvol
Kinders, 2-5 jaar	½- tot 1 teelepel
Kinders, 5-10 jaar	1 tot 2 teelepelsvol
Volwassenes en groter kinders	1 tot 3 teelepelsvol

Gewoonlik verstryk 6 tot 8 uur tussen die toediening van die dosis en die tyd van ontlasting.

Inligting oor Verpakking: Bottels van 4 vloeistof-ons.

PREPARATIONS AND APPLIANCES

THE KUHLMANN CERVICAL TRACTION APPARATUS

The Kuhlmann pneumatic apparatus is a simple appliance for giving traction to the cervical spine. It is a light-weight portable unit, suitable for use in consulting rooms, in the patient's home or the nursing home. It is highly adaptable and may be used in any position selected by the practitioner, sitting, lying or even while the patient is walking around.

The apparatus consists of a comfortable leather cervical halter which is suspended from the chestpiece which works on a pneumatic principle. Traction is applied by squeezing the rubber bulb in a manner similar to the procedure in a Baumanometer. This causes elevation of the horizontal bar of the chestpiece to to the procedure in a Baumanometer. This causes which the halter is attached. A manometer measures the amount of pull in Kilogrammes. A total of 25 Kg. (55 lb.) may be applied.

This method of giving traction has been found very comfortable, and the fact that the patient can control and apply the apparatus himself instills confidence, as the pressure can be reduced by the patient immediately the slighest discomfort is experienced.

By the pneumatic system of applying traction there is a slow gentle stretching of the ligaments, capsule and muscles around the intervertebral joints and time is allowed for relaxation of these tissues. Similarly, on the release of traction the tissues gradually return to their normal position without any jarring of the joint structures.

The Kuhlmann Cervical Traction Apparatus will be found to be invaluable in the treatment of cases of osteo-arthritis with nerve root involvement; also in discogenic lesions in this area.

The price of the complete outfit is £17 10s.

Sole Distributors in Southern Africa: Medical Distributors, 236, Jeppe Street (P.O. Box 3378), Johannesburg.

CIROTYL

Parke Davis Laboratories (Pty.) Limited, the South African subsidiary of Parke, Davis & Company, announce the introduction of Cirotyl, a laxative preparation containing diacetoxydiphenylisatin, a synthetic derivative of diphenylisatin, which has been identified as the active laxative principle of California prunes.

Cirotyl is not absorbed; its mode of action appears to be by contact with the intestinal mucosa, in contrast with other compounds such as anthraquinones and phenolphthalein, which act by contact with the mucosa as well as by absorption and re-excretion in the colon. The action of Cirotyl is gentle but persistent, similar to natural bowel movement.

Indications: Cirotyl is indicated for the prevention and treatment of occasional and habitual constipation; it is especially suitable for the prevention of constipation during convalescent or treatment periods with dietary restriction.

Dosage and Administration: Each teaspoonful (4 c.c.) of Cirotyl contains 1.66 mg. of diacetoxydiphenylisatin in a palatable vehicle.

The following doses, which may be repeated, if necessary, within 24 hours or doubled on the following day are recommended:

Infants	¼ to ½ teaspoonful.
Children 2-5 years	½ to 1 teaspoonful.
Children 5-10 years ...	1 to 2 teaspoonfuls.
Adults and older Children	1 to 3 teaspoonfuls.

The time between the administration of the dose and the time of evacuation is usually 6 to 8 hours.

Package Information: Bottles of 4 fluid ounces.

REVIEWS OF BOOKS

GENITO-URINARY DISEASES

Synopsis of Genitourinary Diseases. By Austin I. Dodson, M.D., F.A.C.S. and J. Edward Hill, M.D. 1956. 6th ed. (Pp. 316+Index. With 124 Illustrations. 41s. 6d.). St. Louis: The C. V. Mosby Company.

The purpose of this concise and well-illustrated handbook is to present and discuss those problems arising in everyday urological practice.

In the early chapters there is a summary of the most prominent signs and symptoms of urogenital diseases; a description of those instruments required in general practice; a brief description of the anatomy of the genito-urinary organs and a general discussion of anomalies. The remaining chapters are arranged largely according to the aetiology of the diseases described. In this (sixth) edition the text has been revised to accommodate recent advances in the application of antibiotics and chemotherapy.

It will be appreciated that this is not a comprehensive textbook but, as its title indicates, it is a *Synopsis*. As such it can be highly recommended as an excellent guide to both medical practitioner and senior student alike.

CANCER OF THE CERVIX

The Laboratory Diagnosis of Cancer of the Cervix. Edited by F. Homburger, M.D. and W. H. Fishman, Ph.D. (Pp. 70. With 25 Figs. 25s.). 1956. Basel and New York: S. Karger. Sole Distributors: P. B. Mayer, Medical Bookseller, P.O. Box 713, Cape Town.

This is the second of a series of *Symposia* on special subjects, the first having been on the *Laboratory Diagnosis of Prostatic Cancer.*

The present volume deals with one of the most vexed problems confronting the present-day gynaecologist and pathologist. The very accessibility of the cervix has brought to bear upon it all the ingenuity of clinician and laboratory worker, the latter with all the diverse technical methods at his disposal. Some of these have led to valuable advances, but their very variety has often resulted in confusion. Each enthusiast for a particular technique is confident that his has solved the problem of early diagnosis. This is particularly true of the Papanicalou-method enthusiasts, who believe that cytology has all the answers. The verbatim discussions following some of the papers indicate clearly that this view-point is opposed by many. The statement in the introduction that only lack of skilled man-power prevents the full application of population screening by cytological methods will hardly arouse wide support.

It is stressed that easier and simpler methods for such screening should be developed, particularly for the *in situ* lesion, which is discussed very fully.

The volume is made up of 9 sections dealing with epidemiology, cytological methods of detection and prognosis, and control of radiotherapy, and with the methods involving beta-glucuronidase activity in the vaginal epithelium and fluid, and their usefulness. The authors of these chapters are leading authorities in their various fields and the present contribution affords a succinct analysis of the overall position. However, it is astonishing that in so comprehensive a survey as this it was not thought feasible to include a section on the now no longer new technique of colpo-microscopy. It is unfortunate that most of the writing on this ingenious and valuable technique appeared in the German, French and Italian literature just before and during the war years, resulting in slow diffusion to the English-speaking world.

The work is beautifully produced and printed and is well illustrated. Not the least of its value is in the comprehensive bibliographies given at the end of each section. It is a survey strongly recommended to the pathologist with a leaning towards gynaecological pathology, and to the scientific gynaecologist.

BLOOD CYTOLOGY

Cytology of the Blood and Blood-Forming Organs. By Marcel Bessis, Director of Research Laboratory, Centre International de Transfusion Sanguine, Paris, France. Translated by Eric Ponder, The Nassau Hospital, Mineola, New York. 1956. (Pp. 629 + xxxii. With 405 Illustrations and 22 full colour plates. $22.00). New York and London: Grune & Stratton, Inc.

The older methods of examining the structure of the formed elements of the blood consist mainly of stained preparations. Stains are not limited to the Romanowsky type—supravital or peroxidase or other stains are commonly employed. In all these methods the preparations are first fixed. It was to be expected that studies of cells in the living state would be undertaken and that the electron microscope would be employed to visualize the ultrastructure of these cells. The author hopes to 'reassess the classical ideas based on stained films by considering them in the light of recent techniques, particularly those of phase microscopy, electron microscopy, cytochemistry, the use of the ultracentrifuge and the examination of the cells by polarized light, by ultra-violet light and the fluorescent microscope'.

More than 20 years ago the reviewer himself studied living blood cells with dark-ground illumination. The single picture in this book by, and the author's opinion of, that method is much less good than was this reviewer's experience. It proved insufficiently useful for cell identification.

The impression left by the various studies of minute structure in this book is that we have not yet learnt enough by these newer methods to identify cells very much better. Spherocytes can be seen as such quite easily in an ordinary wet preparation (or better still in a hanging-drop preparation) and it does not need an electron microscope. Every haematologist has encountered the difficulty when one day he thinks he is dealing with a case of monocytic leukaemia but the next day the case seems clearly to be one of granulocytic leukaemia. The great deal of information presented

in this book will not eliminate difficulties of this kind.

Cells were studied under altered environmental conditions, of temperature, pH, etc. By ultracentrifugation it has been shown that red cells contain within the envelope 3 substances of different densities. By this method the nuclei of granulocytes are seen to occupy a portion of the middle of the cell; in other cells they occupy the lowest part. 'Basophil granules are difficult to sediment'.

There are 16 pages containing 22 coloured plates of blood cells. These are excellent.

It is clear that this book is only for the haematologist. Even he will feel that it is a little disappointing that so much carefully collected data can have so little utilitarian value. These are the days of intense study of cell enzymes. The author's studies are mainly morphological.

DIAGNOSIS OF PROSTATIC CANCER

The Laboratory Diagnosis of Cancer of the Prostate. Edited by F. Homburger, M.D., and W. H. Fishman, Ph.D. (Pp. 51. With 13 Figs. 18s.). S. Karger, A.G., Basel, Switzerland.

Addressed to clinicians, this volume is the first of a series of monographs about the practicable results of research into different problems.

There are three parts. The first two, about the epidemiology and the diagnosis of cancer of the prostate by exfoliative cytology, do not tell the clinicians much, through no fault of the authors. Few epidemiological studies have been done and the study of exfoliated prostatic cells is difficult because of a wide variation in the normal cell types and the presence of atypical cells from the seminal vesicles and elsewhere. Richardson and others (including G. N. Papanicolaou) were only able to find 2 unsuspected cancers, one of which was from the bladder, in a study of 2,000 asymptomatic elderly men, while the expected number should have been between 280-400 if the figures of Rich are accepted. The identification and classification of normal cell types is continuing.

The third and longest part fully justifies the publication of this book. The ordinary methods of estimating the serum acid phosphatase will fail to detect 25-50% of prostatic cancers with skeletal metastases and 80-95% of localized prostatic cancers. Hoping to lower these figures, W. H. Fishman and his co-workers tried out a new method of estimating the level of serum acid phosphatase based on an observation by Abdul-Fadl and King that *l*-tartrate would inhibit the action of acid phosphatase derived from the prostate, liver and spleen, but not that from the red cells. Serum acid phosphatase levels were estimated first in the absence and then in the presence of *l*-tartrate with phenol-phosphate as a substrate and the results were expressed in King-Armstrong units. The difference between the two levels was believed to represent the prostatic fraction of the serum acid phosphatase. Observations on a number of cases, some of which are briefly reported here, showed that the prostatic fraction appeared to be a remarkably sensitive indicator of the presence of early prostatic cancer; indeed the prostatic fraction was often raised before and sometimes without a corresponding rise in the total or conventional serum acid phosphatase level. Cline was able to duplicate these results using a different substrate.

Some of the material in this book was presented at a meeting at the New England Medical Center, and the interesting discussion between biochemists, urologists and others occupies the last 12 pages. There is also a 4-page enclosure about the technical methods used.

Clinicians, especially urologists, and also clinical pathologists will find this book interesting. It is what it sets out to be: an up-to-date account of the most recent diagnostic methods applicable to cancer of the prostate.

CORRESPONDENCE

DOCTORS AND DISPENSING

To the Editor: The state of affairs which affects general practitioners has its repercussion on chemists, who find that they are not making enough money from dispensing. The cause of the trouble lies not with the doctors, as one is led to believe. The shortage of beds in Johannesburg, Durban and Cape Town reflects that hospitals are overcrowded and that the general practitioners have little work. Had these institutions been used only for the poor and needy, as originally intended, they would have sufficed for the needs of each city; but unfortunately, they are invaded by people (in at least 50% of cases) who can well afford to pay a private doctor, their general practitioner.

A visit to Addington Hospital will reveal what well-dressed women come to the Out-Patient Department, in their chauffeur-driven limousines. They pay 2s. for their consultation and often nothing for their treatment. Much of the R.M.O.'s time could be given to truly indigent patients who could do with hospitalization for longer periods, and are turned away because of the shortage of beds.

The livelihood of the farmer, butcher, plumber, business owner, salesman and lawyer are not tampered with by government or provincial administration or by the municipality. My hairdresser who has a little business, makes easily over £120 a month and has some joy in life. These citizens all make a respectable living, for nobody puts spokes in their wheels. In a few years they show an increase in capital and their profits are partly reflected by the purchase of a new car, and improvements or extension of premises; but the general practitioner, with few exceptions, has little to show, except more loss than profit. (I am not speaking of specialists.) It is about time that the organized profession showed a real spirit of fraternity and took a real interest in the welfare of its less fortunate members. In other words, the true spirit of union and medical association should be there.

In face of the ever-increasing number of new general practitioners why cannot some provision be made so that every general practitioner may be assured of a reasonable amount of work so that he will not starve. Otherwise, what is the object of having medical schools and turning out doctors?

Recently, a Medical Benefit Scheme has been advocated for all workmen. Provided it is not a closed panel affair, it should serve its purpose to aid all general practitioners. Unfortunately, it will not stop those who can afford it from seeking advice and treatment from government hospitals when they pay 2s. for a consultation.

As the consultation is so cheap, it is no wonder that the government hospitals are overcrowded and there is often no bed for the really deserving case. The hospital staff complain that they cannot cope with the work. No wonder the institutions run at a staggering loss, to the detriment of the government, taxpayer, doctors and chemists.

The provincial administration or the government with its *overrated charity* and the municipal clinics which give free vaccination to all, are some of the chief causes of the doctors' and chemists' financial distress.

Something should be done by those who profess to have a real and sincere interest in the welfare of the medical profession to rectify this situation. A start should be made with:

1. The virtually free admission of patients to the Government Out-Patient Department. No real investigation is made into the financial status of the patient.

2. Provincial or municipal clinics are sprouting like mushrooms. No discrimination is made to ascertain if the patient or his parents are rich. (Last year my receptionist's uncle died. He was frequently admitted to Addington as a patient. He died a bachelor, leaving an estate of £50,000.)

3. Free vaccination of all and sundry by municipal doctors.

4. Wholesale domiciliary maternity attendance by government district nurses, when many such cases could well afford to pay a general practitioner at least a small fee.

5. General dealers who sell drugs and all sorts of patent medicines, to the detriment of both doctor and chemist.

In the eyes of the chemist, the general practitioner's big crime is that he dispenses some medicine. Yes, in hard times like these, the ordinary general practitioner who has no axe to grind, has to dispense medicines for his non-European patients in order to keep the wolf from the door—and the chemist wants to rob him of such a birthright.

If the Minister of Health decides in favour of chemists, what is going to be the position of many a general practitioner? Will the organized profession or the Government bridge the gap in his finance so that he can balance his monthly budgets? As it is, many of us are having trying times and can hardly make ends meet (an increase in medical fees is out of the question for non-Europeans).

In my own particular case, I may say I am getting on in years. I have had two severe attacks of coronary thrombosis. I am about 50% fit. I do no night work and very few day visits. My practice is 95% non-Europeans—come what may I shall continue to dispense for my poor non-Europeans—and I have not a penny in the bank.

It is time that each member of the profession got a fair chance of earning a living. The old idea, which is still believed by most people today, that the general practitioner is rich, is a myth. There should be a fair distribution of work for every doctor. This realization can only be brought about by the co-operation of both the profession and the Government or the provincial administration, by enforcing drastic changes which may be enumerated as follows:

(a) Much stricter rules for the admission and treatment of patients in government hospitals;

(b) Open Medical Benefit Societies for all workmen with free choice of doctor and chemist—similar to the Typographical Medical Scheme;

(c) As our cities and towns are well provided with hospitals, permanent well-trained nurses and sisters could attend to emergency cases and have the latter refered to hospital, whilst the patient could choose his doctor;

(d) The closing down of clinics which are sprouting all over the country and which are detrimental to the interest of both doctor and chemist.

Last, but not the least, I advocate a compulsory Medical Benefit scheme for all doctors, be they members or not of a Medical Benevolent Society.

Natal. *Medical Practitioner.*

CARCINOMA OF THE UPPER OESOPHAGUS: RESECTION

To the Editor: In your Journal of 21 July 1956, Mr. W. L. Phillips presented an article on *Dysphagia.*

I wish, however, to question a statement he made on p. 361 under the heading *Surgical Treatment.* After stating that carcinoma of the lower third of the oesophagus has a much better prognosis, he goes on: 'It may be stated categorically that carcinoma of the upper and middle thirds of the oesophagus carries so high a surgical mortality rate that many surgeons refuse to carry out resection treatment and prefer to perform "by-pass operations", i.e. the short-circuiting of the carcinomatous site.'

I agree with Mr. Phillips that the mortality rate following resection in the upper thoracic region is higher than for growths lower down, but there is indeed at present very little difference in the mortality rates at these 2 sites in the hands of a number of surgeons. To do a 'by-pass operation' because of the fear of performing resection is to deny the patient his only chance of cure. Indeed, it is not the resection that kills the patient but the procedure as a whole, or perhaps the breakdown of an anastomosis, both of which factors pertain whether the growth is resected or by-passed.

That the proportion of non-resectability is greater with high level lesions is not disputed and if a growth is found to be non-resectable at operation then a by-pass operation is a worthwhile procedure.

In 1952 Sweet [1] reported upon 17 resections for carcinoma of the upper third of the oesophagus with no mortality, and Grimes [2] reported upon 17 cases with 2 deaths. Following supra-aortic anastomoses for middle third carcinomas, Nakayama [3] had no mortality from 14 cases resected through a right thoraco-abdominal approach. Other authors give mortality figures of up to 20%. This is not formidable if one considers the alternative.

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Denis Fuller
Florence Nightingale Bldg.,
Hospital Hill, Johannesburg.

Cortisone vs. Salicylate in Rheumatoid Arthritis

Latest clinical report proves cortisone no better than aspirin in the treatment of rheumatoid arthritis.

On May 29th, 1954, the Joint Committee of the Medical Research Council and Nuffield Foundation published a most significant finding on arthritis therapy—that "for practical purposes" there appears to be "*surprisingly little to choose between cortisone and aspirin.*"[1]

"Sixty-one patients in the early stages of rheumatoid arthritis . . . have been allocated at random to treatment with one or other agent (cortisone 30 cases, aspirin 31 cases) . . .

"Observations made one week, eight weeks, thirteen weeks, and approximately one year after the start of treatment reveal that the two groups have run a closely parallel course in nearly all the recorded characteristics—namely, joint tenderness, range of movement in the wrist, strength of grip, tests of dexterity of hand and foot, and clinical judgments of the activity of the disease and of the patient's functional capacity."[1]

These findings spotlight an earlier report that "aspirin in large doses has definite beneficial results closely akin to those received from ACTH."[2]

High gastric intolerance to aspirin noted among arthritics—a problem easily met by the use of BUFFERIN.

In this latest study, the side-effects recorded for both groups "were equal in the early months of treatment, but *became less in the aspirin group as time passed.*"[1]

Of clinical significance, however, is the high percentage of gastric intolerance to straight aspirin found among the arthritic patients—42% *as against* 3 *to* 10% *variously reported for the general population.*[3, 4]

Earlier investigations reveal the disadvantages of using sodium bicarbonate with aspirin—namely, the lowering of blood salicylate levels and the possible retention of the sodium ion.[2]

BUFFERIN *offers an answer to this problem.*

Unlike straight aspirin, BUFFERIN *is well tolerated, even when given in large doses.*[4]

BUFFERIN contains no sodium. It combines aspirin with two antacid and buffering agents which protect the gastric mucosa against irritation from salicylates—at the same time providing faster absorption of salicylates into the blood stream.

REFERENCES: 1. Brit. Med. J. 1:1223 (May 29) 1954. 2. Med. Times 81:41 (Jan.) 1953. 3. J. Amer. Pharm. Assoc., Sc. Ed. 39:21, 1950. 4. Ind. Med. 20:480 (Oct. 1951.